Hospital Library

# The American Heart Journal

*A Journal for the Study of the Circulation*

Published Monthly Under the Editorial Direction of The American Heart Association

Vol. 20 SEPTEMBER 1940 No. 3

© Am. Ht. Assn.

FRED M. SMITH.....Editor-in-Chief

Associate Editors

HUGH McCULLOCH
IRVING S. WRIGHT
HORACE M. KORNS

EDITORIAL BOARD

EDGAR V. ALLEN
CLAUDE S. BECK
HARRY GOLDBLATT
GEORGE HERRMANN
WILLIAM J. KERR
ROBERT L. LEVY
H. M. MARVIN
JONATHAN C. MEAKINS
ROY W. SCOTT
ISAAC STARR
J. MURRAY STEELE
PAUL D. WHITE
FRANK N. WILSON
CHARLES C. WOLFERTH

Published by THE C. V. MOSBY COMPANY, 3525 Pine Blvd., St. Louis, U. S. A.
Copyright 1940 by The C. V. Mosby Company

Contents on Inside Cover

# The American Heart Journal

## CONTENTS FOR SEPTEMBER, 1940

### Original Communications


The Characteristics of the Chest Lead Electrocardiograms of 100 Normal Adults. Douglas Deeds, M.D., and Arlie R. Barnes, M.D., Rochester, Minn. ---- 261

Phonocardiographic Studies of Early Rheumatic Mitral Disease. Alberto C. Taquini, M.D., Buenos Aires, Argentina, Benedict F. Massell, M.D., and Bernard J. Walsh, M.D., Boston, Mass. ---- 295

Response to Renin of Unanesthetized Normal and Nephrectomized Rats. Arthur Freedman, M.D., Cincinnati, Ohio ---- 304

The Use of "Exercise Tests" in Connection With Venous Pressure Measurements for the Detection of Venous Obstruction in the Upper and Lower Extremities. James Ross Veal, M.D., and Hugh Hudson Hussey, M.D., Washington, D. C. ---- 308

Galvanometric Potentials of the Extremities and of the Thorax in Congenital Dextrocardia. Charles E. Kossmann, M.D., New York, N. Y. ---- 322

The Toxicity of Digitalis and Ouabain in Animals Under Sodium Thiopentobarbital and Sodium Pentobarbital Anesthesia. Charles M. Gruber, M.D., Ph.D., Victor G. Haury, M.D., and Miles E. Drake, Ph.D., Philadelphia, Pa. ---- 329

The Incidence of Syphilitic Aortitis in a Representative Municipal Hospital. Abraham Gelperin, M.D., Cincinnati, Ohio ---- 340

The Cardiovascular System in Pulmonary Tuberculosis. John A. Sweeney, M.D., Philadelphia, Pa. ---- 345

Note on Electrocardiographic Nomenclature. Neuton S. Stern, M.D., Memphis, Tenn. ---- 355


### Department of Clinical Reports


Coarctation of the Aorta in a Child With Arrested Subacute Bacterial Endarteritis and a Calcified Mycotic Aneurysm at the Seat of Stricture. Gertrude H. B. Nicolson, M.D., New York, N. Y. ---- 357

Orthostatic Paroxysmal Auricular Tachycardia With Unusual Response to Change of Posture. M. James Fine, M.D., and Ralph Miller, M.D., Newark, N. J. ---- 366


### Department of Reviews and Abstracts


Selected Abstracts ---- 374

Book Reviews ---- 384

American Heart Association, Inc. ---- 388



Vol. 20, No. 3, September, 1940. The American Heart Journal is published monthly by the C. V. Mosby Company, 3523 Pine Blvd., St. Louis, Mo. Subscription Price: United States, its Possessions, Pan-American Countries, $8.50; Canada, $9.50 a year; Foreign, $9.50. Entered as Second-Class Matter at Post Office at St. Louis, Mo., under Act of March 3, 1879. Printed in the U. S. A.

# The American Heart Journal

VOL. 20 SEPTEMBER, 1940 NO. 3


## Original Communications

### THE CHARACTERISTICS OF THE CHEST LEAD ELECTROCARDIOGRAMS OF 100 NORMAL ADULTS


DOUGLAS DEEDS,* M.D., AND ARLIE R. BARNES, M.D.
ROCHESTER, MINN.


IN 1932, Wolferth and Wood[1] introduced into clinical electrocardiography a precordial lead which rapidly proved to be of extreme value in many pathologic conditions.

Within the limits of variability, the various components of the Wolferth[2, 3, 4] precordial lead have been delineated gradually. As time has passed, the depth of the so-called Q wave that can be considered normal has become less, until now a so-called Q wave whose depth is not less than 2 mm. is considered normal; if it is 1 mm., or less, it is considered definitely abnormal, and, if it is less than 1.4 mm., it is considered as probably abnormal. Notching, slurring, and M or W conformations of the QRS complexes are seen in normal electrocardiograms. The take-off of the RS-T segment may range normally from 0.5 mm. above to 2.0 mm. below the isoelectric line. In normal subjects, aged 15 years or less, the T wave may be upright, but if it is upright in tracings from patients who are more than 15 years of age, it is considered abnormal.[5, 6] T waves more than 9 mm. in depth are seen in the electrocardiograms of normal persons, and therefore are not definitely abnormal.

Concomitantly with this progress, however, confusion has arisen regarding terminology and methods of obtaining the precordial lead electrocardiogram. There are two reasons for this: First, too much latitude has been allowed in methods of application; second, from the standpoint of electrical polarity, Wolferth's lead is literally "upside down" when compared to the standard leads. This is because Wolferth's original method of taking the precordial lead normally results in an inverted T wave. By Wolferth's method, relative positivity of the precordial electrode, that is, a positive electrical potential within the


From the Division of Medicine, The Mayo Clinic.


Abridgment of thesis submitted by Dr. Douglas Deeds to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M. S. in Medicine.


*Fellow in Medicine, The Mayo Foundation.



Received for publication Dec. 9, 1939.

heart, is always represented in the finished tracing by a downward deflection. In a Wolferth precordial lead, the right arm lead wire is attached to the precordial electrode and the left arm or left leg lead wire to the indifferent electrode. In the electrocardiogram so derived, all waves directed downward (for example, the so-called Q wave and the normal T waves) represent relative positivity of the precordial electrode; all waves directed upward (for example, the so-called R wave) represent relative negativity of the precordial electrode.

In the standard, or classical, leads, this arrangement distinctly does not obtain. In Leads I, II, and III, all waves directed downward (for example, the Q and S waves) represent negative electrical potentials within the heart; all waves directed upward (for example, the R and T waves) represent positive electrical potentials in the heart.

Considered in terms of relative positivity or negativity of the precordial electrode, it is apparent that the so-called Q and R waves of Wolferth's precordial lead are in reality R and S waves, respectively, in the proper electrical sense in which we consider these waves in the standard leads. It was inevitable that confusion in terminology should arise under such conditions.

In an attempt to clarify the situation, the American Heart Association[7, 8] recently formulated and published a standard procedure which specifically designates the size of the precordial electrode (not to exceed 3 cm. in diameter), its exact location on the thorax, the position of the indifferent electrode, and a method of application of the lead wire that results in fourth lead waves which are exactly comparable to those of the classical leads. Adherence to the recommendation eliminates the previous source of confusion, for, in these new precordial leads, just as in the standard leads, all upward deflections represent relative positivity of the precordial electrode, and all downward deflections represent relative negativity of the precordial electrode.

Thus, in discussing the standard and new fourth leads, the terms Q, R, S, and T can be used in their correct electrical sense; that is, normally, all Q and S waves are directed downward and all R and T waves are directed upward. Because of its obvious advantages, the immediate and universal acceptance of this standard method of obtaining electrocardiograms is to be most heartily recommended. Realizing that inevitable technical difficulties might discourage the rapid acceptance of this forward step, and believing that normal standards were necessary, the following study was undertaken in October, 1937.

## METHOD OF STUDY

A detailed description of the recommendations of the American Heart Association would be too voluminous to include here. For a clear comprehension of the subject matter to follow, however, some consideration of the technique employed is essential.

*Precordial Electrode.*—The recommendation states that the diameter of the precordial electrode is not to exceed 3 cm. A precordial electrode that complied with this specification was used in this study.

*Location of the Precordial Electrode.*—The recommendation designates six specific locations on the thoracic wall at which the standard electrode is to be placed. Each position is indicated by a subscript; subscript 1 denotes position 1, and so forth. For a detailed description of these positions, the reader is referred to the American Heart Association report.[7] Fig. 1 illustrates these six positions, and the following quotation from the supplementary report of the American Heart Association[8] describes their location.

"The position of the precordial electrode shall be indicated by the subscript used, according to the following plan: subscript 1 shall be used for the right margin of the sternum; 2, for the left margin of the sternum; 3, for a line midway between the left margin of the sternum and the left midclavicular line; 4, for the left midclavicular line; 5, for the left anterior axillary line; and 6, for the left midaxillary line. When the letters and subscripts specified are employed, it shall be understood that in the case of the sternal leads the precordial electrode has been placed in the fourth intercostal space, and that in the case of the other leads it has been placed upon a line drawn from the left sternal margin in the fourth intercostal space to the outer border of the apex beat (or to a point at the junction of the midclavicular line and the fifth intercostal space), and continued around the left side of the chest at the level of the apex beat or of the junction mentioned."

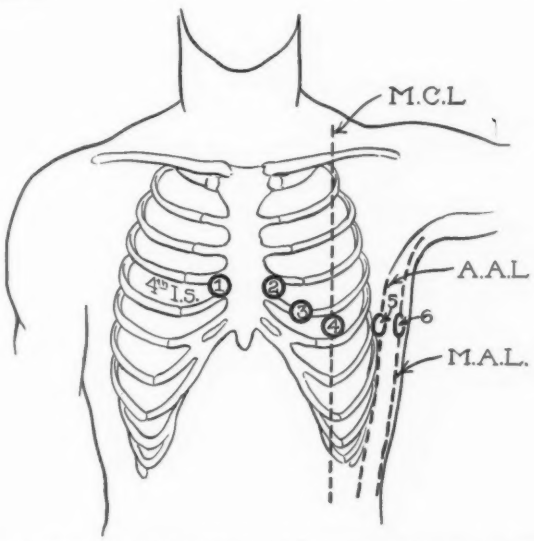



Fig. 1.—Proper points of application of the thoracic electrode to obtain the various CR, CL, and CF thoracic leads. *M.C.L.* denotes midclavicular line; *A.A.L.*, anterior axillary line; *M.A.L.*, midaxillary line; 4th *I.S.*, fourth intercostal space.

*Nomenclature.*—To make the specificity complete, the recommendation creates a new system for the designation of leads, which is outlined in detail. Briefly, the letters used to indicate the various leads specifically determine the position of the indifferent electrode. The letters R, L, F, and B indicate that the indifferent electrode is on the right arm (R), left arm (L), left leg (F, for foot), or back (B) (left paravertebral region), respectively. The letter C indicates that the standard electrode is placed on the thorax in one of the six positions.

Whenever the roman numeral IV is used, it means that the precordial electrode has been placed just at the outer border of the apex beat. The letter T is used

Fig. 2.—Connections of the lead wires with the oscillograph, and the lead selectors which were used in taking leads CR2, CL2, and CF2. The right arm lead wire remains connected to the right arm electrode, and the left leg lead wire remains connected to the precordial electrode until all of the derivations from all six chest positions have been obtained. The left arm lead wire remains connected to the left arm electrode while CL leads are derived, and is then shifted to the left leg electrode when the CF leads are taken. Note that the precordial electrode is not touched until all leads (CR, CL, and CF) have been taken for that particular chest position. It is important that this precaution be observed if one wishes to compare CR, CL, and CF leads quantitatively for a given thoracic position. By a repetition of this method, CR, CL, and CF leads for any thoracic position of the precordial electrode may be obtained rapidly.

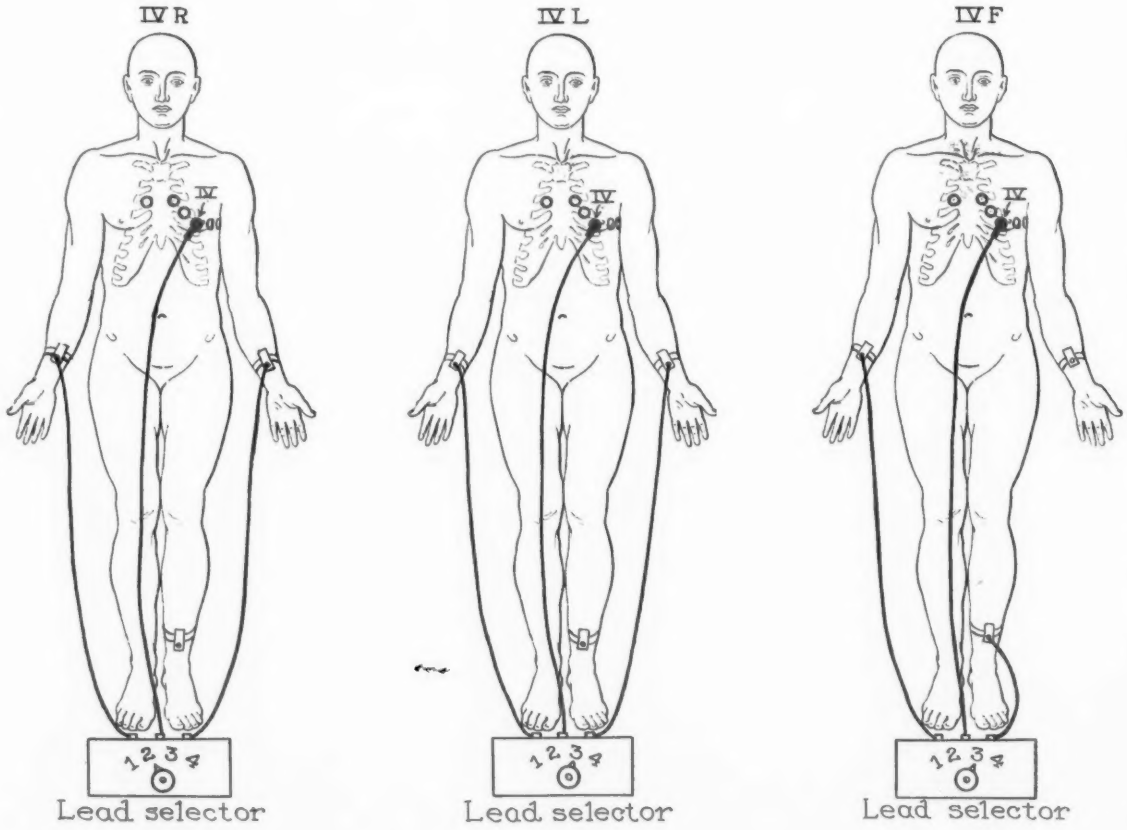



Fig. 3.—Connections of the lead wires with the oscillograph, and the lead selectors which were used in taking Leads IVR, IVL, and IVF. The position marked IV is at a point just outside the cardiac apex.

when the precordial electrode has been paired with a central terminal, connected, through equal resistances of 5,000 ohms, or more, to electrodes on each of the three extremities.

Once the reader is familiar with the new terminology, he can glance at the designation of any given lead and know exactly where the precordial electrode was, and on which part of the body the indifferent electrode was placed.

Let us consider a few examples. The designations $CR_2$, $CL_2$, and $CF_2$ all indicate that the precordial electrode was at position 2 (that is, in the fourth left intercostal space at the left margin of the sternum), and that the indifferent electrode was placed on the right arm (R), the left arm (L), and the left leg (F, for foot), respectively (Fig. 2). The terms $CR_5$, $CL_5$, and $CF_5$ indicate the respective sites of the indifferent electrodes and that the precordial electrode is now at position 5 (anterior axillary line). When the letters IVR, IVL, and IVF are used, it is immediately apparent that the precordial electrode is at the outer border of the apex beat (IV), and that the indifferent electrode is on the right arm, left arm, and left leg, respectively (Fig. 3).

Another quotation from the committee's recommendation is in order: "It will be noted that Leads $CF_4$ and IVF (or Lead $CR_4$ and Lead IVR) may sometimes be identical. In the case of the latter (Lead IVF or Lead IVR), however, the precordial electrode is placed at the outer border of the cardiac apex regardless of the position of the apex with reference to the bony landmarks of the chest, whereas, in the case of the former (Lead $CF_4$ or Lead $CR_4$), this electrode is placed in the midclavicular line even when the cardiac apex is far to the left of this position."

## TECHNIQUE

All electrocardiograms were recorded by Victor Model A (oscillograph type) electrocardiographs. Frequent standardizations were performed to maintain a constant deflection of 1 cm. per millivolt. A suitable electrode paste was used to insure good contact with the skin. This was found to be of vital importance in obtaining a satisfactory and uniform contact for the precordial electrode.

At all times, the derivations used in this study were obtained in such a manner as to conform exactly to the recommendations of the American Heart Association.[7, 8] The precordial electrode which was used measured exactly 3 cm. in diameter. The new nomenclature was employed throughout, and at all times the technique was so arranged that, except for the Wolferth leads, the presence of a relatively positive electrical potential at the precordial electrode was represented in the finished tracing by an upward deflection.

## MATERIAL FOR STUDY

A preliminary study was made on ten apparently healthy and normal adults (six men and four women) who ranged in age from 21 to 33 years, with an average age of 26.9 years. Only those whose history was free from even a suggestion of cardiac disease or an attack of rheumatic fever, who had normal blood pressure and a heart of normal size and configuration, as ascertained by stereoscopic roentgenograms of the thorax, were considered normal. The standard Leads I, II, and III were taken in the usual fashion.

In taking the multiple precordial leads, a long, perforated, elastic thoracic band was used. It was fastened in place by means of hooks on the flat, rectangular electrode which was an integral part of the band. This band was fitted snugly about the thorax in such a way that posteriorly the attached electrode was in contact with the skin of the back just to the left of the spine at about the level of the angle of the scapula; anteriorly the six precordial positions were covered by the elastic strap. The posterior electrode was used as the indifferent electrode

in obtaining Lead IVB and the Wolferth leads. Anteriorly, the band held the 3-centimeter electrode firmly in place at any desired location.

The skin at position 1 was prepared by rubbing a suitable electrode paste into the skin where the electrode was to be placed. The importance of a suitable, conductive electrode paste cannot be minimized. Comparing Fig. 4*A* (no paste) with Fig. 4*B* (with paste), we see easily the marked change that results when good contact is achieved by means of paste. The amplitude is markedly increased, and, in other instances, the "abnormal" S-T segment which was obtained when paste was not used was even more striking than that shown in Fig. 4*A*. A comparison of Lead $CR_1$ when taken from dry skin, rubbed with plain water, and skin rubbed with electrode paste is shown in Fig. 4*B* ($CR_1$ dry; $CR_1$ wet; $CR_1$ with paste).

After the skin had been prepared, the precordial electrode was placed at position 1, and, without disturbing the lead wires of the right and left arms, the lead wire from the left leg was disconnected from its electrode and attached to the precordial electrode.

With the lead selector on Lead II (right arm lead wire to left leg lead wire), Lead $CR_1$ was obtained. Simply by switching the lead selector to Lead III (left arm lead wire to left leg lead wire), Lead $CL_1$ was recorded.

With the lead selector still on Lead III, and without disturbing anything else, the single maneuver of disconnecting the left arm lead wire from the left arm electrode and reconnecting it to the left leg electrode produced Lead $CF_1$.

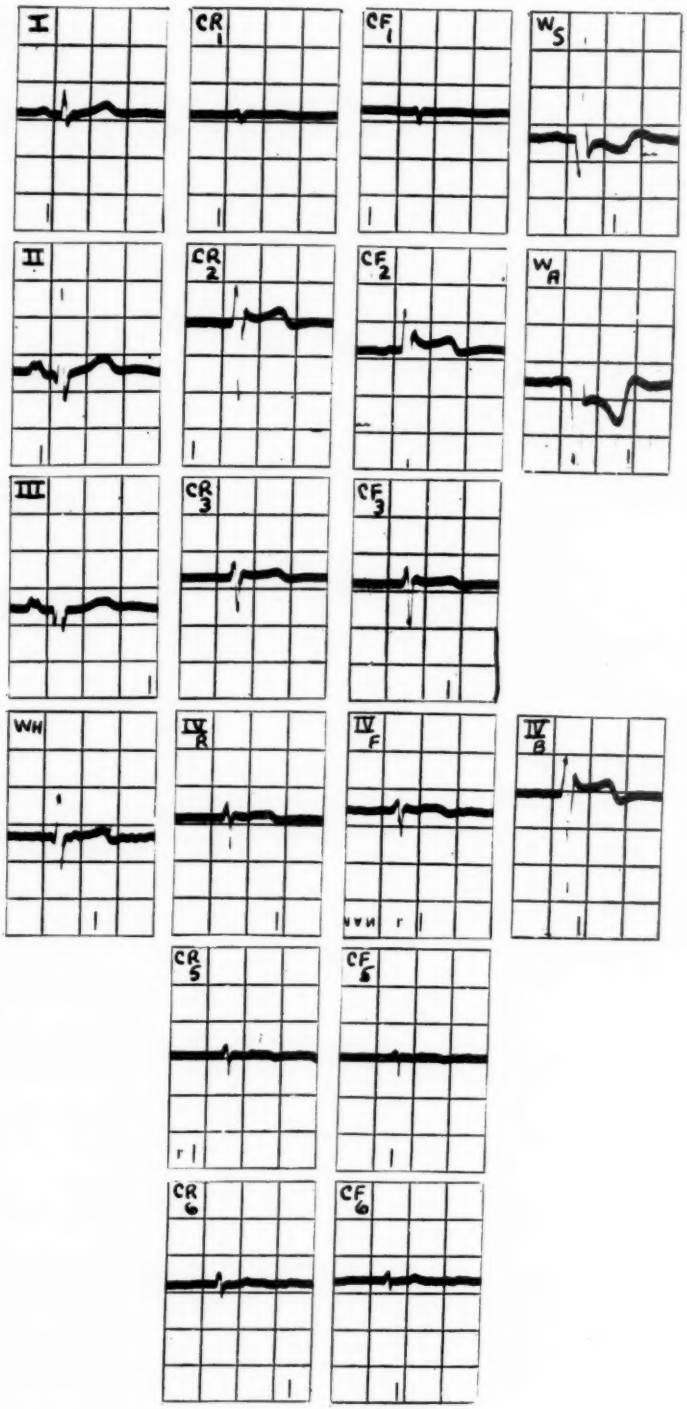
Thus, Leads $CR_1$, $CL_1$, and $CF_1$ were derived with a minimum of effort. As soon as $CF_1$ was completed, the left arm lead wire was returned to its normal position on the left arm. The precordial electrode, with the left leg lead wire attached, was moved to the freshly prepared position 2. With the lead selector first on Lead II, and then on Lead III, Leads $CR_2$ and $CL_2$, respectively, were rapidly obtained. With the lead selector still on Lead III, the left arm lead wire was again shifted to the left leg electrode, and Lead $CF_2$ was obtained, following which the left arm lead wire was returned to its normal position to be ready for the next series of three derivations.

Utilizing this system, CR, CL, and CF leads, at positions 1 to 6, inclusive, were rapidly obtained as the precordial electrode was shifted from one to another of the six thoracic locations. As soon as all six CR, CL, and CF leads were finished, the limb electrodes were permanently removed.

The Whitten lead was taken next. The right arm electrode, with the corresponding lead wire attached, was placed in the right axilla on a level with the heart. Similarly, the left arm electrode, attached to its lead wire, was placed in the left axilla. By this means, with the lead selector on Lead I, the Whitten lead,[9] or an amplified Lead I, is obtained.

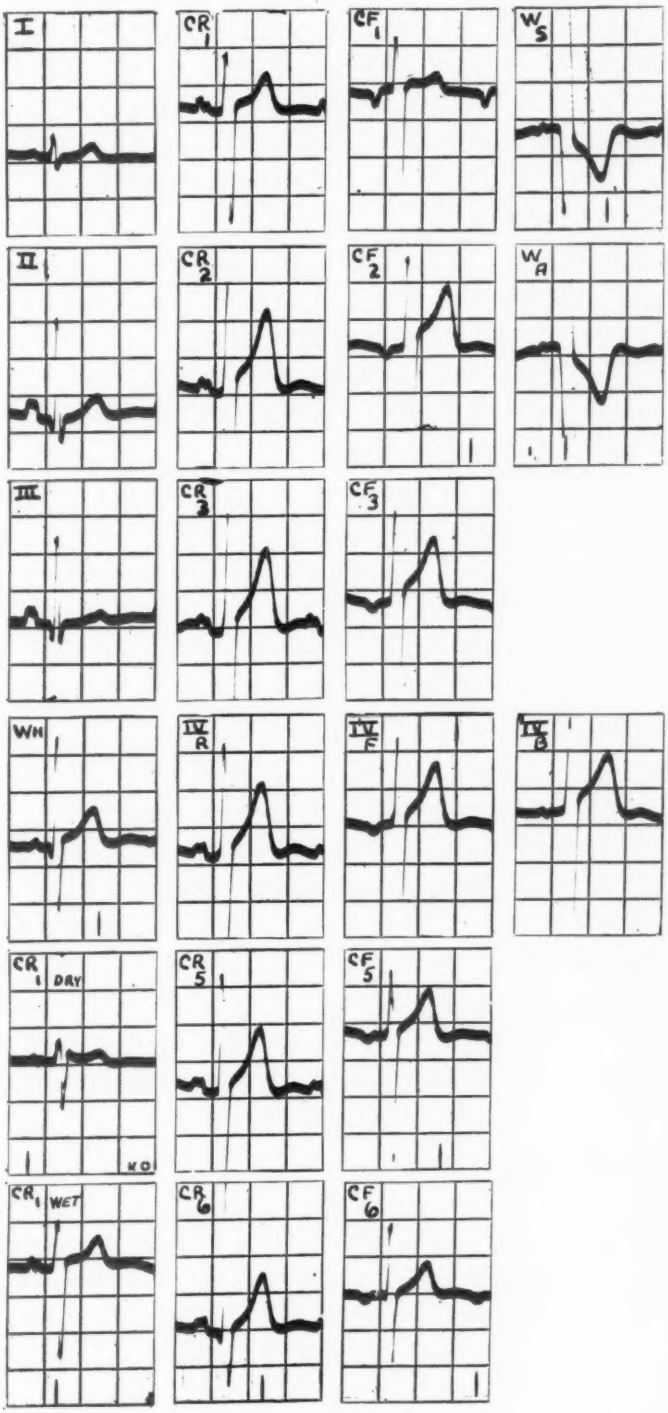
Next, the Wolferth precordial anteroposterior thoracic leads were obtained. Two such thoracic leads were taken to permit comparison with the changes which occurred when the precordial electrode was shifted from position 2 to a location just outside the apex beat. The right arm lead wire was connected to the precordial electrode which was formerly used in the laboratory (8 cm. in diameter), and this electrode was placed with its center at position 3. The left arm wire was connected to the indifferent electrode previously described, which was situated to the left of the vertebral column at about the level of the angle of the scapula. This arrangement resulted in what was designated "Wolferth standard," as this had been the "standard" type of Wolferth lead previously in use in the laboratory.

To compare the relative effect, if any, of using this large electrode, the standard 3-centimeter precordial electrode was then placed at position 2, with the right arm lead wire attached to it, and the lead designated as "Wolferth" (small electrode at position 2) was obtained.




*A.*

Fig. 4.—Electrocardiogram of a normal man. Thoracic lead electrocardiograms obtained (*A*) without and (*B*) with the use of an electrode paste. Note that, by using the paste, not only is there an increase in the amplitude of the deflections, but also that certain S-T segment contours that appear abnormal in the tracings obtained without the use of the paste have disappeared. The nomenclature of lead designations is explained in the text.


I
CR 1
CF 1
W S
II
CR 2
CF 2
W A
III
CR 3
CF 3
WH
IV R
IV F
IV B
CR 1 DRY
NO
CR 5
CF 5
CR 1 WET
CR 6
CF 6

*B.*

The lead designated as "Wolferth apex" was derived by moving the small precordial electrode with its attached right arm lead wire from position 2 to the outer border of the apex beat, so that it occupied exactly the same position as it did when Leads IVR, IVL, and IVF were taken.

Finally, by leaving the electrodes in the position they occupied for taking the Wolferth apex lead, and by simply reversing the attachments of the right and left arm lead wires, so that the right arm wire was now connected to the posterior electrode and the left arm wire to the apical electrode, Lead IVB was obtained.

Thus, on each of these ten normal subjects the following leads were available for study: I; II; III; $CR_1$, $CL_1$, $CF_1$; $CR_2$, $CL_2$, $CF_2$; $CR_3$, $CL_3$, $CF_3$; IVR, IVL, IVF (the electrode was always placed at the outer border of the apex, so that IVR, IVL, and IVF, rather than $CR_4$, $CL_4$, and $CF_4$, would be obtained); $CR_5$, $CL_5$, $CF_5$; $CR_6$, $CL_6$, $CF_6$; Whitten (WH); Wolferth Standard (WS); Wolferth (small electrode at position 2); Wolferth apex (WA); and IVB.

Figs. 5 and 6 illustrate typical series on a man and a woman, respectively. The Wolferth lead (small electrode at position 2) was not included in the illustration, for this lead was taken merely to ascertain whether the use of the 3-centimeter electrode resulted in exactly the same tracing as that which was obtained when the large, old-style electrode was used. By actual comparison, it soon became apparent that the small electrode did *not* affect the tracings obtained from normal subjects.

The P, Q, R, S, and T waves, and the relation of the take-off of the S-T segment to both the P-R and T-P base lines of each of these derivations in the tracings from each subject in this group, were accurately measured, recorded, and tabulated as to maximal, minimal, and average amplitude. The average P-R and QRS intervals were recorded for each lead, also. The average values for the various leads are shown in Table I.

In the recommendation, the committee stated: "It is suggested for all ordinary purposes that Lead IVR or Lead IVF be employed. The latter lead should have preference until it has been established that the former, which is somewhat more convenient, is equivalent to the latter for all practical purposes, or yields results of equal value."

From Table I it is evident that, quantitatively, the CR, CL, and CF leads are *not* interchangeable. It is apparent that the CR leads give the greatest amplitude, and CF leads, the least. The P waves were usually comparable to those of the standard leads when Leads CR and CL were used, but usually were inverted or diphasic in CF leads.

As these conclusions were based on such a small series, a more comprehensive study on 100 normal adults was undertaken. Because of the time, technical aid, and large quantity of film required, it seemed advisable to compare only two, instead of all three, CR, CL, and CF leads. The recommendation just quoted, and the convenience and seeming anatomic soundness of the CR leads as compared to the CL leads, plus the other aforementioned factors, led to selection of the CR and CF leads for comparison in the larger series. This series comprised fifty men and fifty women, all of whom met the requirements laid down for the preliminary survey on the ten normal adults.

TABLE I

SUMMARY OF THE STUDY OF THE STANDARD ELECTROCARDIOGRAMS AND PRECORDIAL LEADS ON TEN NORMAL ADULTS (THIS SERIES INCLUDES CL LEADS)*

| LEAD | P WAVE | | Q WAVE | | R WAVE | | S WAVE | | T WAVE | | DEVIATION OF S-T SEGMENT | | | | P-R INTERVAL, AVERAGE DURATION, MM. | AVERAGE DURATION OF QRS, MM. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | FROM P-R | | FROM T-P | | | |
| | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | | |
| I | +10 | +0.4 | − 3<br>0= 7 | −0.4 | +10 | + 6.2 | − 9<br>0= 1 | − 1.1 | +10 | +2.0 | + 6<br>0= 4 | +0.2 | 0=10 | 0 | 0.14 | 0.07 |
| II | +10 | +0.9 | − 4<br>0= 6 | −0.5 | +10 | +12.9 | − 7<br>0= 3 | − 1.9 | +10 | +2.4 | + 4<br>− 2<br>0= 4 | +0.9<br>−0.5 | + 2<br>− 6<br>0= 2 | +0.3<br>−0.3 | 0.15 | 0.07 |
| III | +10 | +0.5 | − 5<br>0= 5 | −0.6 | +10 | + 6.3 | − 6<br>0= 4 | − 1.2 | + 7<br>− 1<br>di 2 | +0.8<br>−0.8 | + 3<br>− 1<br>0= 6 | +0.3<br>−0.2 | + 6<br>− 5<br>0= 4 | +0.3<br>−0.2 | 0.15 | 0.08 |
| $CR_1$ | +10 | +0.9 | 0=10 | 0.0 | +10 | + 4.4 | −10 | − 9.7 | + 9<br>so 1 | +3.0 | +10 | +0.9 | + 8<br>0= 2 | +0.6 | 0.15 | 0.08 |
| $CR_2$ | +10 | +1.0 | 0=10 | 0.0 | +10 | + 8.4 | −10 | −16.9 | +10 | +9.3 | +10 | +1.9 | + 9<br>0= 1 | +1.7 | 0.15 | 0.08 |
| $CR_3$# | +9 | +0.9 | 0= 9 | 0.0 | + 9 | +10.5 | − 9 | −14.3 | + 9 | +9.8 | + 9 | +1.9 | + 9 | +1.6 | 0.15 | 0.08 |
| IVR | +10 | +1.0 | 0=10 | 0.0 | +10 | +15.5 | −10 | −11.7 | +10 | +9.0 | + 9<br>0= 1 | +1.6 | + 9<br>− 1 | +1.2<br>−1.0 | 0.15 | 0.08 |
| $CR_5$ | +10 | +1.0 | − 4<br>0= 6 | −0.6 | +10 | +27.4 | −10 | −6.46 | +10 | +7.5 | + 8<br>− 2 | +1.0<br>−0.5 | + 8<br>− 2 | +0.8<br>−1.0 | 0.15 | 0.08 |
| $CR_6$ | +10 | +0.9 | − 7<br>0= 3 | −0.8 | +10 | +24.1 | − 9<br>0= 1 | − 2.1 | +10 | +4.7 | + 6<br>− 1<br>0= 3 | +0.5<br>−0.3 | + 5<br>− 2<br>0= 3 | +0.3<br>−0.6 | 0.14 | 0.08 |

TABLE I—CONT'D

| LEAD | P WAVE | | Q WAVE | | R WAVE | | S WAVE | | T WAVE | | DEVIATION OF S-T SEGMENT | | | | P-R INTERVAL, AVERAGE DURATION, MM. | AVERAGE DURATION OF QRS, MM. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | FROM P-R | | FROM T-P | | | |
| | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | | |
| $CL_1$ | +5<br>di 5 | +0.6 | 0=10 | 0.0 | +10 | + 3.3 | −10 | −12.8 | + 4<br>- 3<br>di 3 | +2.0<br>−0.8 | + 9<br>0= 1 | +0.9 | + 9<br>0= 1 | +0.7 | 0.14 | 0.08 |
| $CL_2$ | +10 | +0.5 | 0=10 | 0.0 | +10 | + 7.2 | −10 | −17.9 | +10 | +6.3 | +10 | +1.9 | +10 | +1.5 | 0.14 | 0.08 |
| $CL_3$# | +9 | +0.5 | 0= 9 | 0.0 | + 9 | + 7.4 | - 9 | −14.5 | + 9 | +7.4 | + 8<br>0= 1 | +1.8 | + 9 | +1.6 | 0.14 | 0.08 |
| IVL | +10 | +0.5 | 0=10 | 0.0 | +10 | +10.6 | −10 | −10.8 | +10 | +6.1 | + 9<br>0= 1 | +1.3 | + 9<br>- 1 | +1.1<br>−0.7 | 0.14 | 0.08 |
| $CL_5$ | +10 | +0.4 | - 3<br>0= 7 | −1.1 | +10 | +21.2 | −10 | - 5.5 | +10 | +5.2 | + 7<br>- 2<br>0= 1 | +0.7<br>−0.4 | + 7<br>- 2<br>0= 1 | +0.7<br>−0.6 | 0.15 | 0.08 |
| $CL_6$ | +10 | +0.4 | - 6<br>0= 4 | −0.9 | +10 | +18.9 | - 7<br>0= 3 | - 1.0 | +10 | +2.8 | + 4<br>- 1<br>0= 5 | +0.5<br>−0.2 | + 4<br>- 1<br>0= 5 | +0.3<br>−0.2 | 0.15 | 0.07 |
| $CF_1$ | +2<br>−4<br>di 4 | +0.8<br>−0.9 | 0=10 | 0.0 | +10 | + 2.6 | −10 | −18.3 | + 4<br>- 6 | +1.9<br>−1.0 | + 9<br>0= 1 | +0.9 | + 9<br>0= 1 | +0.9 | 0.14 | 0.08 |
| $CF_2$ | +2<br>−4<br>di 4 | +0.7<br>−0.5 | 0=10 | 0.0 | +10 | + 6.4 | −10 | −23.7 | +10 | +6.0 | +10 | +1.9 | +10 | +1.9 | 0.13 | 0.08 |
| $CF_3$# | +2<br>−2<br>di 5 | +0.3<br>−0.4 | - 1<br>0= 8 | −0.4 | + 9 | + 6.9 | - 9 | −16.5 | + 9 | +6.7 | + 9 | +1.8 | + 9 | +1.8 | 0.14 | 0.08 |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| IVF | +4<br>−2<br>di 4 | +0.3<br>−0.3 | − 1<br>0= 9 | −1.2 | +10 | + 7.5 | −10 | −13.1 | +10 | +5.9 | +10 | +1.9 | +10 | +1.9 | 0.13 | 0.08 |
| $CF_5$ | +4<br>−2<br>di 4 | +0.5<br>−0.3 | − 4<br>0= 6 | −1.0 | +10 | +19.3 | −10 | − 7.0 | +10 | +4.8 | + 8<br>− 2 | +0.7<br>−0.4 | + 8<br>− 2 | +0.7<br>−0.4 | 0.14 | 0.07 |
| $CF_6$ | +2<br>−1<br>di 7 | +0.4<br>−0.2 | − 7<br>0= 3 | −1.2 | +10 | +13.1 | − 8<br>0= 2 | − 2.2 | +10 | +2.5 | + 4<br>− 2<br>0= 4 | +0.4<br>−0.2 | + 5<br>− 2<br>0= 3 | +0.3<br>−0.2 | 0.14 | 0.07 |
| Wolferth standard | −6<br>di 4 | −0.5 | 0=10 | 0.0 | −10 | − 8.3 | +10 | +20.3 | −10 | −7.5 | −10 | −2.0 | −10 | −1.8 | 0.15 | 0.08 |
| Wolferth sm. elec. #2 | −6<br>di 4 | −0.5 | 0=10 | 0.0 | −10 | − 8.0 | +10 | +19.2 | −10 | −7.1 | −10 | −2.0 | −10 | −1.8 | 0.15 | 0.08 |
| Wolferth apex | −7<br>di 3 | −0.4 | + 1<br>0= 9 | +0.2 | −10 | −12.5 | +10 | +13.0 | −10 | −6.0 | −10 | −1.2 | − 9<br>0= 1 | −1.2 | 0.15 | 0.08 |
| IVB | +9<br>poly 1 | +0.4 | − 1<br>0= 9 | −0.2 | +10 | +13.1 | −10 | +12.5 | +10 | +6.8 | +10 | +1.1 | + 9<br>0= 1 | +1.0 | 0.15 | 0.08 |
| Whitten | +10 | +0.7 | − 7<br>0.3 | −3.4 | +10 | +22.8 | − 8<br>0= 2 | − 1.1 | +10 | +4.1 | + 6<br>− 2<br>0= 2 | +0.5<br>−0.4 | + 4<br>− 2<br>0= 4 | +0.4<br>−0.8 | 0.14 | 0.08 |

*The sign "+" indicates that the deflection is directed upward from the base line.

The sign "−" indicates that the deflection is directed downward from the base line.

The letters "di" indicate that the deflection was diphasic.

The numeral "0" indicates that no deflection, for the wave designated, occurred.

The syllable "poly" denotes that the deflection was polyphasic.

The sign "#" indicates that, because of the peculiar contour of the heart, position $C_3$ coincided with position 4 on the chest of one female. Hence, $CR_3$, $CL_6$ and $CF_3$ tracings were obtained on only nine patients of this series.

The sign "=" in such an expression as "0 = 7" means that the designated deflection was absent seven times.

The letters "iso" indicate that the deflection was isoelectric.

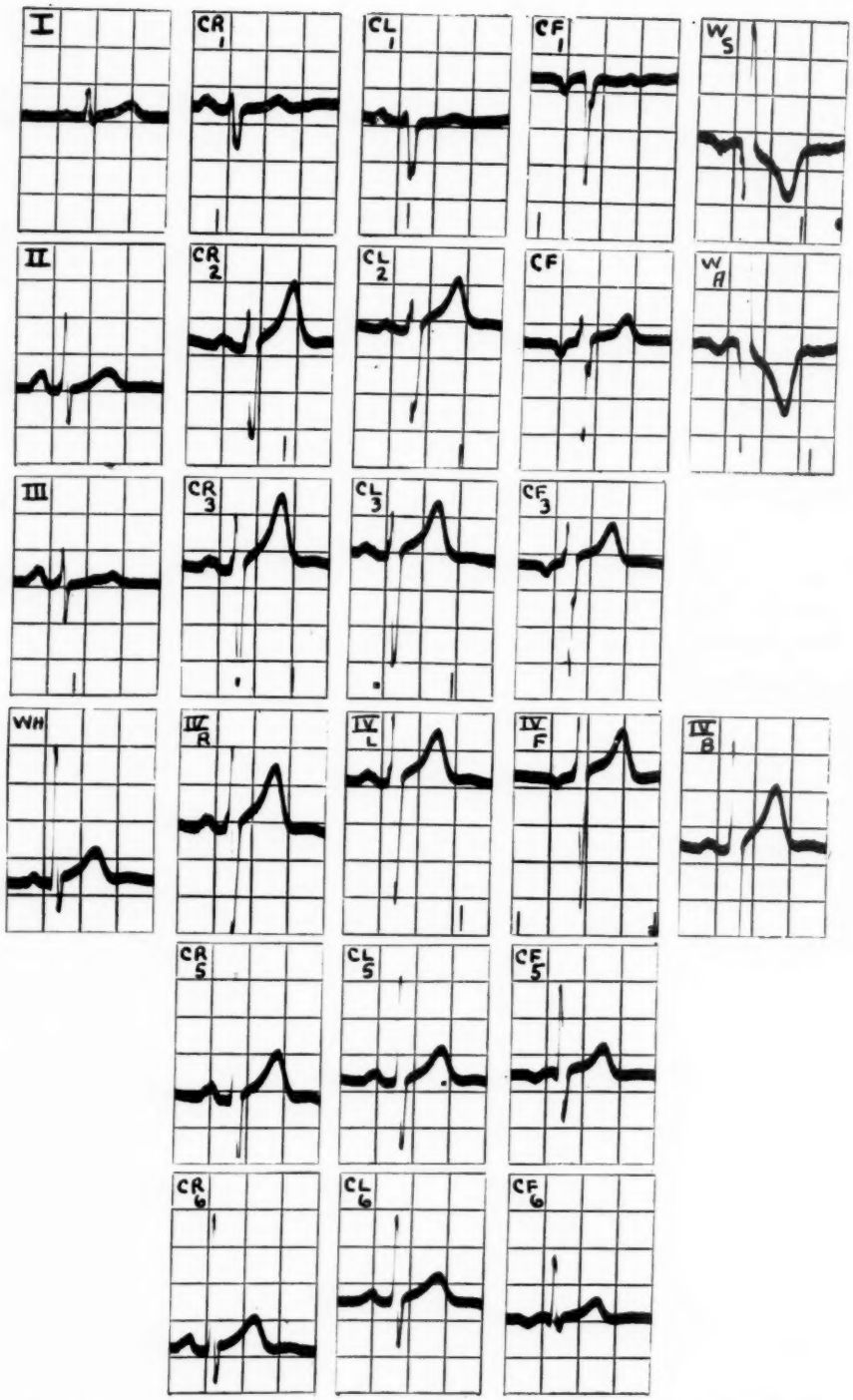



Fig. 5.—An average example of the entire series of standard and thoracic lead electrocardiograms, obtained from a normal man. At a given position, the three leads, CR, CL, and CF, were taken before the thoracic electrode was moved. Note that changing the location of the indifferent electrode results in some variation in the electrocardiograms which are obtained with any given position of the thoracic electrode.

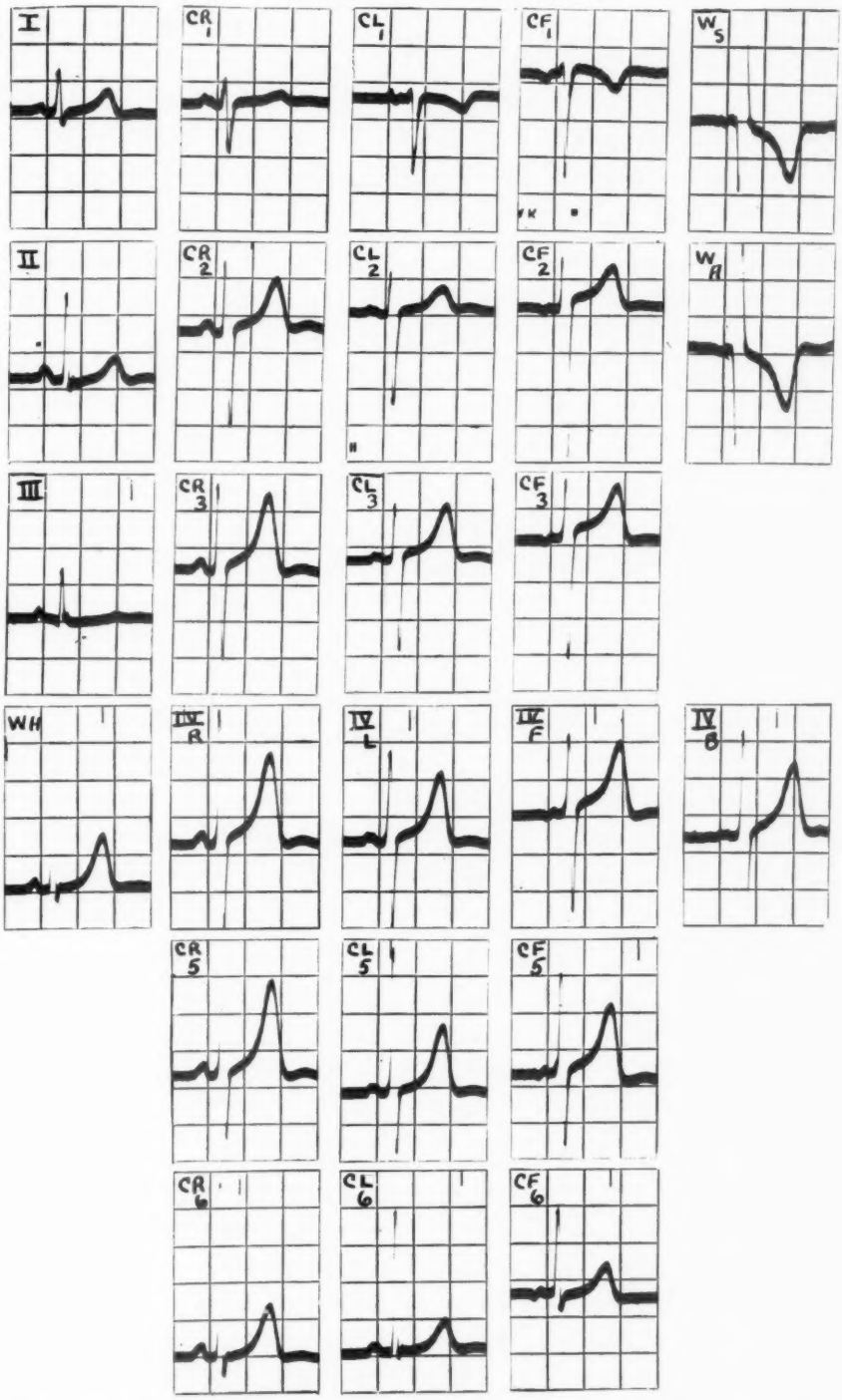



Fig. 6.—An average example of the entire series of standard and thoracic lead electrocardiograms, obtained from a normal woman.

The ages of these one hundred normal adults varied from a minimum of 17 years to a maximum of 47 years. The average age for the entire group was 28.4 years. No attempt was made to select subjects of an average habitus.

The various electrocardiograms were obtained as they were in the preliminary study, except that Wolferth leads (with the small electrode at position 2) and CL leads were not taken.

The fact that CL leads were not taken simplified the technique somewhat. As soon as the standard leads were finished, the left arm electrode was permanently disconnected. With the right arm lead wire connected to the right arm and the left arm lead wire connected to the left leg, the left leg lead wire was attached to the precordial electrode. With this arrangement of the lead wires, and with the precordial electrode at position 1, Lead $CR_1$ was obtained when the lead selector was placed on Lead II, and Lead $CF_1$ was obtained when it was placed on Lead III. Thus, Leads CR and CF, 1 to 6, were rapidly derived by the simple maneuvers of moving the precordial electrode from one position to another, and switching the lead selector to Lead II for the CR leads and to Lead III for the CF lead. As before, Leads IVR and IVF were taken in all cases in which the apex beat was palpable.

Thus, on each subject, the following leads were available for analysis: I, II, III; $CR_1$ and $CF_1$; $CR_2$ and $CF_2$; $CR_3$ and $CF_3$; IVR and IVF (the electrode was always placed at the outer border of the apex, so that IVR and IVF, rather than $CR_4$ and $CF_4$, would be obtained); $CR_5$ and $CF_5$; $CR_6$ and $CF_6$; Whitten (WH); Wolferth (Standard) (WS); Wolferth apex (WA); IVB and standardization (ST). Each lead was subjected to the same careful quantitative analysis as in the preliminary series of ten subjects, and the final measurements were recorded in tabular form.

Table II shows the direction and average amplitude of the various deflections, as well as the average conduction times in the series of fifty normal adult men. Table III is a similar summary of the observations on fifty normal adult women. Table IV summarizes the final averages for both men and women. Tables V and VI supply the maximal and minimal values of the amplitudes of the various deflections for fifty men and fifty women.*

*P Wave.*—As a rule, in CR and CL leads the P wave is upright. In CF leads it is usually inverted or diphasic. "Notching" of the P wave was very commonly encountered. If slight indentations are considered as "notching," this feature occurred in more than 90 per cent of the cases.

*Q Wave.*—A true Q wave is rare at the first three positions; it occurred only once in $CR_1$, once in $CR_3$, and once in $CF_3$. The farther to the left the electrode is moved, the more common and pronounced this wave becomes. The so-called Q wave of the Wolferth leads is designated as an R wave in this discussion, because that is what it really is. A true Q wave was frequently present at the fourth, fifth, and sixth positions (Fig. 7), and occasionally a true Q wave (an initial upward deflection of the QRS complex) was discernible in the Wolferth apex lead (Fig. 7).

*Because of the short distance from the apical impulse to the sternal border in one of the women, no third position could be used without marked overlapping of positions 2 and 4. In this case, therefore, $CR_3$, $CL_6$ and $CF_3$ leads were *not* obtained. Thus, all components total only 49 or 99, respectively, when third position derivations are being considered.

*R Wave.*—The amplitude of the R wave is greater in all of the CR leads than in the CL and CF leads. It is apparent that the R wave in CL, CF, and Wolferth leads (so-called Q wave in the latter) will exhibit a significant decrease in amplitude, or will even disappear completely, more readily than will the R wave in the CR leads. The smallest R (so-called Q) wave in the Wolferth standard lead measured 1.0 mm. (WS in Fig. 8). In this same lead and in the same individuals, R waves frequently measured 2.3 mm. ($WS_1$ in Fig. 8). In the Wolferth leads, the R (so-called Q) wave is usually longer at position 4 than at position 2. Occasionally, however, the reverse was observed.

*S Wave.*—Nothing specific can be said regarding the S wave that is not apparent from the tables. Its range of variability is tremendous.

*T Wave.*—At position 1 the T wave is rarely negative, but it is frequently diphasic in the CR leads; it is slightly more commonly negative or diphasic in CL leads, and is usually negative or diphasic in CF leads. At all other positions it was always upright, except at position 6, where it was rarely diphasic or polyphasic, but never actually inverted. With one exception, the T wave in all Wolferth leads was normally inverted. This exception occurred in the case of a woman in the standard Wolferth derivation. This subject's apex beat was situated at the site ordinarily reserved for position 3. Therefore, position 3 was not available. This subject was perfectly healthy, and she had passed through pregnancy and parturition without incident. All of the leads in this case were retaken, but re-examination of them failed to reveal this pathologic T wave in the Wolferth lead. It is interesting to note that, in this case, when a Wolferth anteroposterior lead was taken with the standard electrode at position 2 (fourth intercostal space) and when additional anteroposterior leads were taken with the precordial electrode in the second or third intercostal space parasternally, the T waves were all inverted (normal). However, when the electrode was placed high in the epigastric notch, over the xiphoid, the T wave was again abnormally upright. The fact that the T wave at position 2 was originally upright was *not* the result of placing the electrode too low over the heart.

In the case of one man, marked notching of the T wave in IVF occurred; this was less evident in IVB (Fig. 9). It is interesting that notching of the T wave was more marked in IVB than it was in the Wolferth apex lead, although the latter is obtained in exactly the same manner as IVB; the only difference is that the lead wires are reversed. In the standard leads in the case of one man (Fig. 10), there were a diphasic T wave in Lead I, frankly inverted T waves in Leads II and III, and a diphasic tendency in some of the T waves in the precordial leads. Another man (Fig. 11) had a diphasic T wave in Lead II and a frankly inverted, almost "cove-plane," T wave in Lead III. The nearest thing to negativity of a T wave at position 2 in the precordial leads was observed in a woman (Fig. 12, Lead $CF_2$).

TABLE II

SUMMARY OF THE STUDY OF THE STANDARD ELECTROCARDIOGRAMS AND PRECORDIAL LEADS ON FIFTY NORMAL MALES (CL LEADS WERE NOT STUDIED IN THIS SERIES)*

| LEAD | P WAVE | | Q WAVE | | R WAVE | | S WAVE | | T WAVE | | DEVIATION OF S-T SEGMENT | | | | P-R INTERVAL, AVERAGE DURATION, MM. | AVERAGE DURATION OF QRS, MM. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | FROM P-R | | FROM T-P | | | |
| | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | | |
| I | +50 | +0.5 | −17<br>0=33 | −0.4 | +50 | + 6.4 | −42<br>0= 8 | − 1.9 | +49<br>di 1 | + 2.5 | +33<br>− 3<br>0=14 | +0.3<br>−0.1 | +12<br>− 9<br>0=29 | +0.3<br>−0.2 | 0.14 | 0.09 |
| II | +50 | +1.1 | −25<br>0=25 | −0.6 | +50 | +12.1 | −41<br>0= 9 | − 2.8 | +47<br>− 1<br>di 2 | + 3.1<br>− 1.3 | +41<br>− 6<br>0= 3 | +0.5<br>−0.6 | +18<br>−17<br>0=15 | +0.4<br>−0.5 | 0.16 | 0.08 |
| III | +44<br>− 3<br>di 3 | +0.7<br>−0.3 | −30<br>0=20 | −0.9 | +50 | + 7.1 | −36<br>0=14 | − 2.6 | +35<br>di 8 | + 1.2<br>− 1.0 | +32<br>−11<br>0= 7 | +0.3<br>−0.2 | +10<br>−20<br>0=20 | +0.3<br>−0.4 | 0.15 | 0.08 |
| $CR_1$ | +49<br>− 1<br>di 0 | +1.0<br>−0.3 | − 1<br>0=49 | −0.0 | +49<br>0= 1 | + 5.0 | −49<br>0= 1 | −10.1 | +47<br>− 1<br>di 2 | + 3.3<br>− 0.4 | +50 | +1.0 | +42<br>− 1<br>0= 7 | +0.8<br>−0.1 | 0.15 | 0.08 |
| $CR_2$ | +48<br>di 2 | +1.1 | 0 | 0.0 | +50 | +10.9 | −50 | −19.6 | +50 | + 9.8 | +50 | +2.1 | +49<br>− 1 | +1.7<br>−0.3 | 0.15 | 0.08 |
| $CR_3$ | +49<br>di 1 | +1.1 | − 1<br>0=49 | −0.2 | +50 | +13.0 | −50 | −17.9 | +50 | +10.3 | +50 | +2.1 | +49<br>0= 1 | +1.8 | 0.15 | 0.08 |
| IVR | +49<br>di 1 | +1.1 | − 5<br>0=45 | −0.5 | +50 | +19.2 | −50 | −13.8 | +50 | + 9.9 | +49<br>0= 1 | +1.7 | +48<br>− 1<br>0= 1 | +1.3<br>−0.4 | 0.15 | 0.08 |
| $CR_5$ | +49<br>iso 1 | +1.2 | −19<br>0=31 | −0.7 | +50 | +26.4 | −49<br>0= 1 | − 8.2 | +50 | + 8.3 | +47<br>− 1<br>0= 2 | +1.1<br>−0.4 | +40<br>− 5<br>0= 5 | +0.9<br>−0.3 | 0.15 | 0.08 |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $CR_6$ | +49<br>iso 1 | +1.2 | −37<br>0=13 | −1.0 | +50 | +14.6 | −50 | − 4.1 | +49<br>di 1 | + 5.9 | +43<br>− 4<br>0= 3 | +0.7<br>−0.3 | +30<br>− 9<br>0=11 | +0.6<br>−0.4 | 0.15 | 0.08 |
| $CF_1$ | + 5<br>−36<br>di 9 | +0.8<br>−0.3 | 0 | 0.0 | +50 | + 3.3 | −50 | −17.0 | +16<br>−29<br>di 5 | + 2.2<br>−1.9 | +43<br>− 4<br>0= 3 | +0.7<br>−0.2 | +45<br>− 2<br>0= 3 | +0.7<br>−0.1 | 0.14 | 0.08 |
| $CF_2$ | +13<br>−25<br>di 12 | +0.4<br>−0.6 | 0 | 0.0 | +50 | + 8.4 | −50 | −25.4 | +50 | + 7.1 | +50 | +1.9 | +50 | +1.9 | 0.14 | 0.09 |
| $CF_3$ | +13<br>−17<br>di 20 | +0.4<br>−0.5 | − 1<br>0=49 | −1.4 | +50 | + 9.2 | −50 | −21.1 | +50 | + 7.5 | +50 | +1.8 | +50 | +1.8 | 0.14 | 0.08 |
| IVF | +17<br>−16<br>di 17 | +0.4<br>−0.4 | − 3<br>0=47 | −0.8 | +50 | +11.8 | −50 | −14.5 | +50 | + 7.0 | +49<br>− 1 | +1.3<br>−0.2 | +49<br>0= 1 | +1.4 | 0.14 | 0.08 |
| $CF_5$ | +19<br>− 8<br>di 23 | +0.4<br>−0.4 | −16<br>0=34 | −0.7 | +50 | +16.4 | −50 | − 7.4 | +50 | + 5.4 | +40<br>− 2<br>0= 8 | +0.7<br>−0.7 | +44<br>− 2<br>0= 4 | +0.7<br>−0.7 | 0.15 | 0.08 |
| $CF_6$ | +17<br>−13<br>di 20 | +0.3<br>−0.3 | −33<br>0=17 | −1.0 | +50 | +13.4 | −37<br>0=13 | − 2.5 | +48<br>di 2 | + 2.8 | +21<br>−13<br>0= 16 | +0.3<br>−0.2 | +31<br>− 5<br>0=14 | +0.3<br>−0.2 | 0.15 | 0.07 |
| Wolferth standard | −48<br>di 2 | −0.5 | 0.0 | 0 | −50 | −10.9 | +50 | +23.6 | −50 | − 8.6 | −50 | −2.3 | −48<br>0= 2 | −2.1 | 0.16 | 0.09 |
| Wolferth apex | −49<br>di 1 | −0.5 | + 1<br>0=49 | +0.3 | −50 | −15.3 | +50 | +17.1 | −50 | − 8.6 | −50 | −1.8 | −50 | −1.6 | 0.16 | 0.08 |
| IVB | +49<br>di 1 | +0.5 | − 1<br>0=49 | −0.1 | +50 | +15.6 | −50 | −16.2 | +50 | + 8.6 | +50 | +1.7 | +50 | +1.5 | 0.16 | 0.08 |
| Whitten | +49<br>di 1 | +0.9 | −42<br>0= 8 | −1.0 | +50 | +21.1 | −42<br>0= 8 | − 3.2 | +48<br>− 0<br>poly 2 | + 5.1 | +30<br>−13<br>0= 7 | +0.6<br>−0.3 | +23<br>−17<br>0=10 | +0.5<br>−0.5 | 0.14 | 0.08 |

*The signs have the same significance as they have in Table I.

TABLE III

SUMMARY OF THE STUDY OF THE STANDARD ELECTROCARDIOGRAMS AND PRECORDIAL LEADS ON FIFTY NORMAL ADULT FEMALES (CL LEADS WERE NOT STUDIED IN THIS SERIES)*

| LEAD | P WAVE | | Q WAVE | | R WAVE | | S WAVE | | T WAVE | | DEVIATION OF S-T SEGMENT | | | | P-R INTERVAL, AVERAGE DURATION, MM. | AVERAGE DURATION OF QRS, MM. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | FROM P-R | | FROM T-P | | | |
| | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | | |
| I | +50 | +0.5 | −11<br>0=39 | −0.2 | +50 | + 4.8 | −39<br>0=11 | − 1.1 | +50 | +1.7 | +25<br>- 8<br>0=17 | +0.2<br>−0.1 | + 5<br>−19<br>0=26 | +0.0<br>−0.1 | 0.14 | 0.07 |
| II | +50 | +1.2 | −24<br>0=26 | −0.5 | +50 | +11.1 | −35<br>0=15 | − 1.9 | +50 | +2.2 | +17<br>−18<br>0=15 | +0.3<br>−0.3 | + 3<br>−35<br>0=12 | +0.0<br>−0.6 | 0.15 | 0.08 |
| III | +47<br>di 3 | +0.7 | −33<br>0=17 | −0.8 | +50 | + 7.0 | −30<br>0=20 | − 1.5 | +25<br>- 5<br>di 20 | +1.0<br>−1.0 | +15<br>−18<br>0=17 | +0.2<br>−0.2 | + 4<br>−34<br>0=12 | +0.1<br>−0.4 | 0.15 | 0.07 |
| $CR_1$ | +49<br>di 1 | +0.9 | 0.0 | 0.0 | +48<br>0= 2 | + 3.2 | −50 | − 9.3 | +43<br>- 0<br>di 7 | +1.8 | +47<br>0= 3 | +0.6 | +35<br>- 6<br>0= 9 | +0.4<br>−0.3 | 0.15 | 0.08 |
| $CR_2$ | +50 | +1.0 | 0.0 | 0.0 | +50 | + 5.9 | −50 | −16.6 | +50 | +6.2 | +50 | +1.3 | +45<br>- 2<br>0= 3 | +0.9<br>−0.4 | 0.15 | 0.08 |
| $CR_3$# | +49 | +1.1 | 0.0 | 0.0 | +49 | + 7.7 | −49 | −13.8 | +49 | +7.0 | +49 | +1.2 | +43<br>- 4<br>0= 2 | +0.8<br>−0.2 | 0.15 | 0.08 |
| IVR | +50 | +1.1 | 0.0 | 0.0 | +50 | +11.7 | −50 | −11.0 | +50 | +7.7 | +48<br>- 1<br>0= 1 | +1.1<br>−0.0 | +43<br>- 5<br>0= 2 | +0.7<br>−0.6 | 0.15 | 0.08 |
| $CR_5$ | +50 | +1.2 | - 9<br>0=41 | −0.6 | +50 | +21.5 | −47<br>0= 3 | − 5.4 | +50 | +7.1 | +41<br>- 5<br>0= 4 | +0.6<br>−0.4 | +31<br>−12<br>0= 7 | +0.4<br>−0.5 | 0.15 | 0.08 |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $CR_6$ | +49<br>− 1 | +1.2<br>−0.6 | −25<br>0=25 | −0.7 | +50 | +10.3 | −34<br>0=16 | − 2.9 | +50 | +5.3 | +34<br>−10<br>0= 6 | +0.4<br>−0.3 | +17<br>−22<br>0=11 | +0.3<br>−0.4 | 0.15 | 0.07 |
| $CF_1$ | + 1<br>−38<br>di 11 | +0.3<br>−0.8 | 0.0 | 0.0 | +48<br>0= 2 | + 2.1 | −50 | −17.8 | + 5<br>−36<br>di 9 | +1.7<br>−1.7 | +45<br>− 2<br>0= 3 | +0.6<br>−0.8 | +46<br>− 1<br>0= 3 | +0.6<br>−0.3 | 0.13 | 0.08 |
| $CF_2$ | + 6<br>−26<br>di 18 | +0.8<br>−0.5 | 0.0 | 0.0 | +50 | + 4.6 | −50 | −24.5 | +49<br>− 0<br>di 1 | +4.3 | +49<br>0= 1 | +1.3 | +48<br>− 1<br>0= 1 | +1.3<br>−0.2 | 0.13 | 0.08 |
| $CF_3$# | + 7<br>−23<br>di 19 | +0.3<br>−0.5 | 0.0 | 0.0 | +49 | + 5.3 | −49 | −19.7 | +49 | +4.8 | +47<br>0= 2 | +1.2 | +47<br>− 1<br>0= 1 | +1.3<br>−0.2 | 0.13 | 0.08 |
| IVF | + 7<br>−17<br>di 26 | +0.4<br>−0.4 | 0.0 | 0.0 | +50 | + 7.3 | −50 | −14.3 | +50 | +5.4 | +48<br>0= 2 | +1.0 | +48<br>− 2 | +1.0<br>−0.1 | 0.14 | 0.08 |
| $CF_5$ | + 7<br>−11<br>di 32 | +4<br>−0.3 | − 3<br>0=47 | −0.5 | +50 | +12.0 | −46<br>0= 4 | − 5.8 | +50 | +4.7 | +33<br>− 6<br>0=11 | +0.5<br>−0.3 | +38<br>− 6<br>0= 6 | +0.5<br>−0.3 | 0.14 | 0.07 |
| $CF_6$ | + 6<br>− 9<br>di 35 | +0.5<br>−0.2 | −24<br>0=26 | −0.4 | +50 | + 9.9 | −36<br>0=14 | − 2.0 | +50 | +2.8 | +22<br>−11<br>0=17 | +0.2<br>−0.2 | +29<br>− 5<br>0=16 | +0.3<br>−0.5 | 0.14 | 0.07 |
| Wolferth standard | −42<br>di 8 | −0.4 | 0.0 | 0.0 | −50 | − 5.6 | +50 | +17.8 | + 1<br>−49 | +1.1<br>−4.2 | −48<br>0= 2 | −1.2 | + 2<br>−47<br>0= 1 | +0.1<br>−1.1 | 0.15 | 0.08 |
| Wolferth apex | + 1<br>−42<br>di 7 | +0.1<br>−0.4 | 0.0 | 0.0 | −50 | − 9.5 | +50 | +14.6 | −50 | −6.1 | −49<br>0= 1 | −1.0 | + 1<br>−47<br>0= 2 | +0.1<br>−0.9 | 0.14 | 0.08 |
| IVB | +42<br>di 8 | +0.4 | 0.0 | 0.0 | +50 | + 9.9 | −50 | −14.0 | +50 | +6.2 | +48<br>0= 2 | +1.0 | +47<br>− 3 | +0.9<br>−0.1 | 0.15 | 0.08 |
| Whitten | +50 | +2.2 | −37<br>0=13 | −0.6 | +50 | +17.2 | −30<br>0=20 | − 1.5 | +50 | +4.2 | +32<br>− 8<br>0=10 | +0.2<br>−0.2 | +13<br>−17<br>0=20 | +0.2<br>−0.3 | 0.14 | 0.08 |

*The signs have the same significance as in Table I, except that the sign # needs further comment, as follows. Because of the unusual contour of the heart, position $C_3$ coincided with position 4 on the chest of one female. Hence, $CR_3$ and $CF_3$ tracings were available on only forty-nine patients of this series.

TABLE IV

SUMMARY OF THE STUDY OF THE STANDARD ELECTROCARDIOGRAMS AND PRECORDIAL LEADS ON FIFTY NORMAL ADULT MALES AND FIFTY NORMAL ADULT FEMALES (CL LEADS WERE NOT STUDIED IN THIS SERIES)*

| LEAD | P WAVE | | Q WAVE | | R WAVE | | S WAVE | | T WAVE | | DEVIATION OF S-T SEGMENT | | | | P-R INTERVAL, AVERAGE DURATION, MM. | AVERAGE DURATION OF QRS, MM. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | FROM P-R | | FROM T-P | | | |
| | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEFLECTION | AVERAGE AMPLITUDE, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | DIRECTION OF DEVIATION | AVERAGE DEVIATION, MM. | | |
| I | +100 | +0.5 | −28<br>0=72 | −0.3 | +100 | + 5.6 | − 81<br>0= 19 | − 1.5 | + 99<br>di 1 | +2.1 | + 58<br>− 11<br>0= 31 | +0.2<br>−0.1 | +17<br>−28<br>0=55 | +0.1<br>−0.2 | 0.14 | 0.08 |
| II | +100 | +1.2 | −49<br>0=51 | −0.5 | +100 | +11.6 | − 76<br>0= 24 | − 2.4 | + 97<br>− 1<br>di 2 | +2.6<br>−1.3 | + 58<br>− 24<br>0= 18 | +0.4<br>−0.5 | +21<br>−52<br>0=27 | +0.2<br>−0.5 | 0.155 | 0.08 |
| III | + 91<br>− 3<br>di 6 | +0.7<br>−0.3 | −63<br>0=37 | −0.9 | +100 | + 7.1 | − 66<br>0= 34 | − 2.1 | + 60<br>− 12<br>di 28 | +1.1<br>−1.0 | + 47<br>− 29<br>0= 24 | +0.2<br>−0.2 | +14<br>−52<br>0=32 | +0.2<br>−0.4 | 0.15 | 0.075 |
| $CR_1$ | + 98<br>− 1<br>di 1 | +0.9<br>−0.3 | − 1<br>0=99 | −0.0 | + 97<br>0= 3 | + 4.1 | − 99<br>0= 1 | − 9.7 | + 90<br>− 1<br>di 9 | +2.5<br>−0.4 | + 97<br>0= 3 | +0.8 | +77<br>− 7<br>0=16 | +0.6<br>−0.2 | 0.15 | 0.08 |
| $CR_2$ | + 98<br>− 0<br>di 2 | +1.1 | 0=100 | 0.0 | +100 | + 8.4 | −100 | −18.1 | +100 | +8.0 | +100 | +1.7 | +94<br>− 3<br>0= 3 | +1.3<br>−0.3 | 0.15 | 0.08 |
| $CR_3$# | + 98<br>di 1 | +1.1 | − 1<br>0=98 | −0.2 | + 99 | +10.3 | − 99 | −15.9 | + 99 | +8.6 | + 99 | +1.6 | +92<br>− 4<br>0= 3 | +1.3<br>−0.2 | 0.15 | 0.08 |
| IVR | + 99<br>di 1 | +1.1 | − 5<br>0=95 | −0.5 | +100 | +15.5 | −100 | −12.4 | +100 | +8.8 | + 97<br>− 1<br>0= 2 | +1.4<br>−0.0 | +91<br>− 6<br>0= 3 | +1.0<br>−0.5 | 0.15 | 0.08 |
| $CR_5$ | + 99<br>iso 1 | +1.2 | −28<br>0=72 | −0.6 | +100 | +24.0 | − 96<br>0= 4 | − 6.8 | +100 | +7.7 | + 88<br>− 6<br>0= 6 | +0.8<br>−0.4 | +71<br>−17<br>0=12 | +0.6<br>−0.4 | 0.15 | 0.08 |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $CR_6$ | + 98<br>− 1<br>iso 1 | +1.2<br>−0.6 | −62<br>0=38 | −0.8 | +100 | +12.4 | − 73<br>0= 27 | − 3.5 | + 99<br>poly 1 | +5.6 | + 77<br>− 14<br>0= 9 | +0.6<br>−0.3 | +47<br>−31<br>0=22 | +0.5<br>−0.4 | 0.15 | 0.075 |
| $CF_1$ | + 6<br>− 74<br>di 20 | +0.5<br>−0.5 | 0=100 | 0.0 | + 98<br>0= 2 | + 2.7 | −100 | −17.4 | + 21<br>− 65<br>di 14 | +2.0<br>−1.8 | + 88<br>− 6<br>0= 6 | +0.6<br>−0.1 | +91<br>− 3<br>0= 6 | +0.6<br>−0.2 | 0.135 | 0.08 |
| $CF_2$ | + 19<br>− 51<br>di 30 | +0.6<br>−0.5 | 0=100 | 0.0 | +100 | + 6.5 | −100 | −24.9 | + 99<br>di 1 | +5.7 | + 99<br>0= 1 | +1.6 | +98<br>− 1<br>0= 1 | +1.6<br>−0.2 | 0.135 | 0.085 |
| $CF_3$# | + 20<br>− 40<br>di 39 | +0.4<br>−0.5 | − 1<br>0=98 | −1.4 | + 99 | + 7.2 | − 99 | −20.4 | + 99 | +6.2 | + 97<br>0= 2 | +1.5 | +97<br>− 1<br>0= 1 | +1.5<br>−0.2 | 0.135 | 0.08 |
| IVF | + 24<br>− 33<br>di 43 | +0.4<br>−0.4 | − 3<br>0=97 | −0.8 | +100 | + 9.6 | −100 | −14.4 | +100 | +6.2 | + 97<br>− 1<br>0= 2 | +1.1<br>−0.2 | +97<br>− 2<br>0= 1 | +1.2<br>−0.1 | 0.14 | 0.08 |
| $CF_5$ | + 26<br>− 19<br>di 55 | +0.4<br>−0.3 | −19<br>0=81 | −0.6 | +100 | +14.2 | − 96<br>0= 4 | − 6.6 | +100 | +5.0 | + 73<br>− 8<br>0= 19 | +0.6<br>−0.5 | +82<br>− 8<br>0=10 | +0.6<br>−0.5 | 0.145 | 0.07 |
| $CF_6$ | + 23<br>− 22<br>di 55 | +4<br>−0.3 | −57<br>0=43 | −0.7 | +100 | +11.7 | − 73<br>0= 27 | − 2.2 | + 98<br>di 2 | +2.8 | + 43<br>− 24<br>0= 33 | +0.2<br>−0.2 | +60<br>−10<br>0=30 | +0.3<br>−0.3 | 0.145 | 0.07 |
| Wolferth standard | − 90<br>di 10 | −0.5 | 0=100 | 0.0 | −100 | − 8.2 | +100 | +20.7 | + 1<br>− 99 | +1.1<br>−6.4 | − 98<br>0= 2 | −1.8 | + 2<br>−95<br>0= 3 | +0.1<br>−1.6 | 0.155 | 0.08 |
| Wolferth apex | + 1<br>− 91<br>di 8 | +0.1<br>−0.5 | − 1<br>0=99 | −0.3 | −100 | −12.4 | +100 | +15.8 | −100 | −7.4 | − 99<br>0= 1 | −1.4 | + 1<br>−97<br>0= 2 | +0.1<br>−1.2 | 0.15 | 0.08 |
| IVB | + 91<br>di 9 | +0.5 | − 1<br>0=99 | −0.1 | +100 | +12.8 | −100 | −15.1 | +100 | +7.4 | + 98<br>0= 2 | +1.4 | +97<br>− 3 | +1.2<br>−0.1 | 0.155 | 0.08 |
| Whitten | + 99<br>di 1 | +1.5 | −79<br>0=21 | −0.8 | +100 | +19.1 | −72<br>0=28 | − 2.4 | + 98<br>poly 2 | +4.7 | + 62<br>− 21<br>0= 17 | +0.4<br>−0.3 | +36<br>−34<br>0=30 | +0.3<br>−0.4 | 0.14 | 0.08 |

*The signs have the same significance as in Table I, except that sign # needs further comment, as follows. Because of the peculiar contour of the heart, position $C_3$ coincided with position 4 on the chest of one female. Hence $CR_3$ and $CF_3$ tracings were available on only ninety-nine patients of this series.

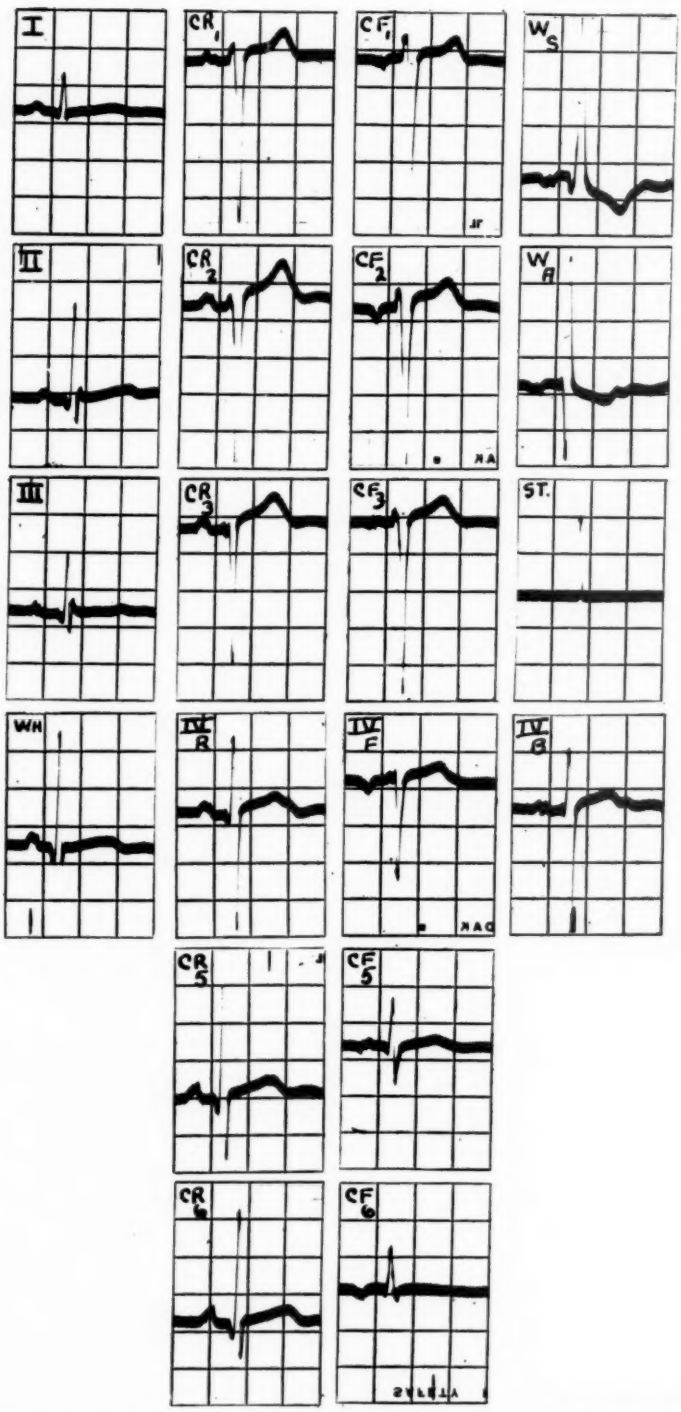



Fig. 7.—Electrocardiogram of a normal man. A true Q wave occurs in IVR, $CR_5$, $CR_6$, $CF_5$, and $CF_6$. A very slight Q wave is present in the Wolferth apex (WA) lead.

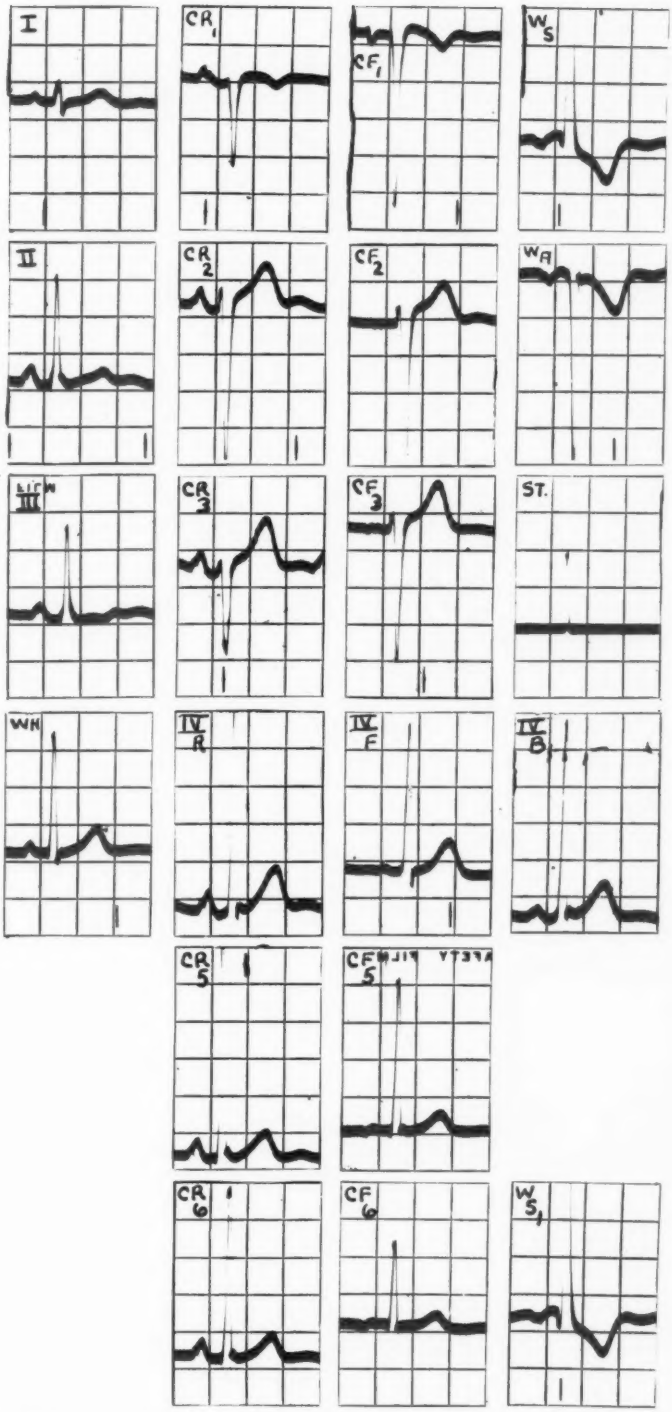



Fig. 8.—Electrocardiogram of a normal man. This illustrates the smallest R wave (so-called Q wave, measuring 1.0 mm.) in the Wolferth standard lead (WS) which was observed in the entire series. Frequently, the R wave (so-called Q wave) in this individual Wolferth standard lead was 2.3 mm. in amplitude (see $WS_1$) in complexes adjacent to those in which the R wave (so-called Q wave) had an amplitude of only 1 mm. Note the small amplitude of the S wave in Leads IVR and IVF.

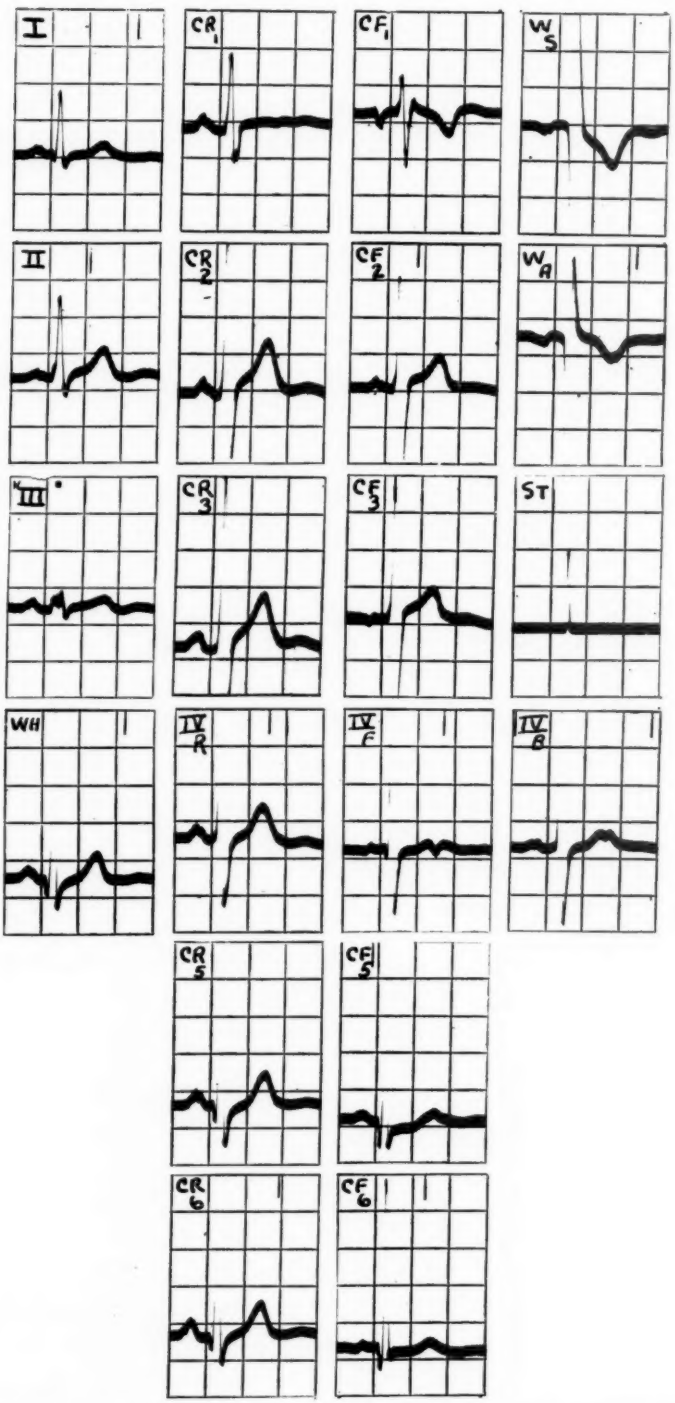



Fig. 9.—Electrocardiogram of a normal man. Leads IVF and IVB illustrate the only frankly notched T waves which were encountered in any of the precordial leads of the entire series. Note that the T wave in the Wolferth lead taken at the apex is only very slightly indented, when compared with IVB.

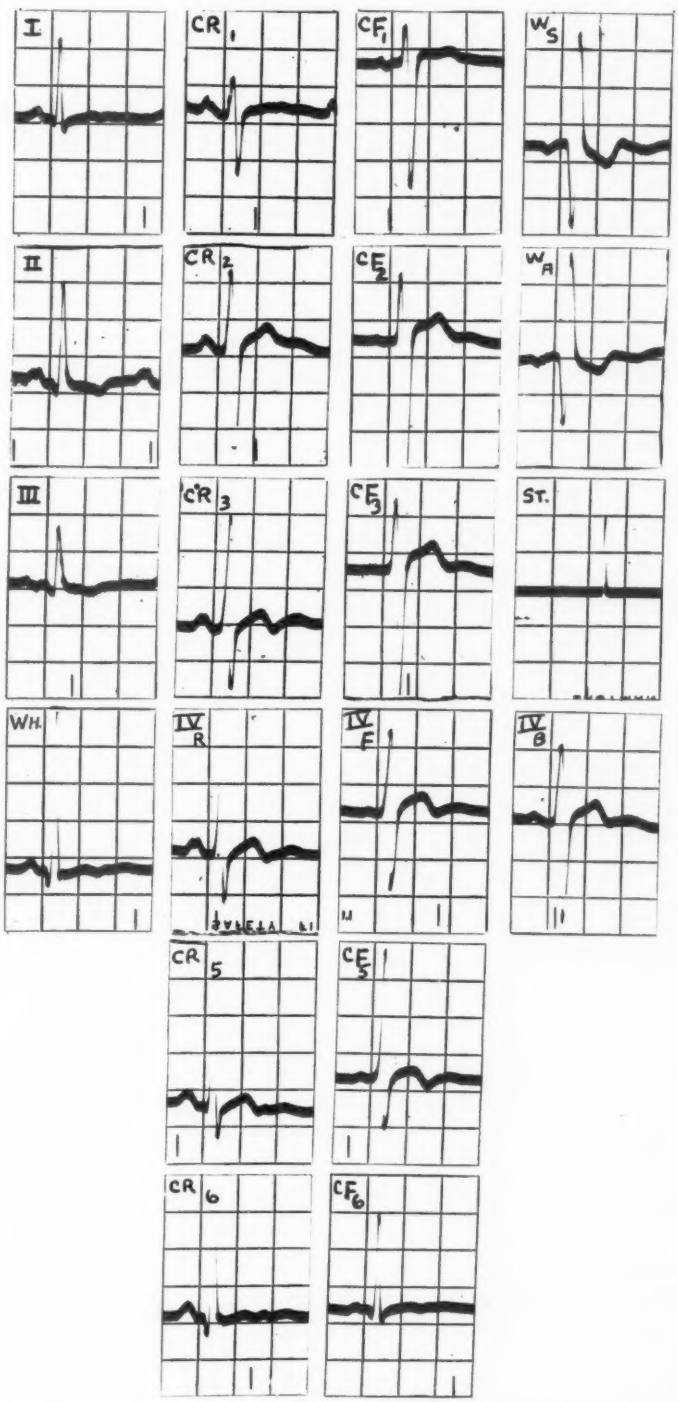



Fig. 10.—Electrocardiogram of a normal man. Note that the T wave is diphasic in Lead I and inverted in Leads II and III, and that it has a diphasic tendency in IVR, IVF, $CF_5$, Wolferth standard (WS), Wolferth apex (WA), and IVB.

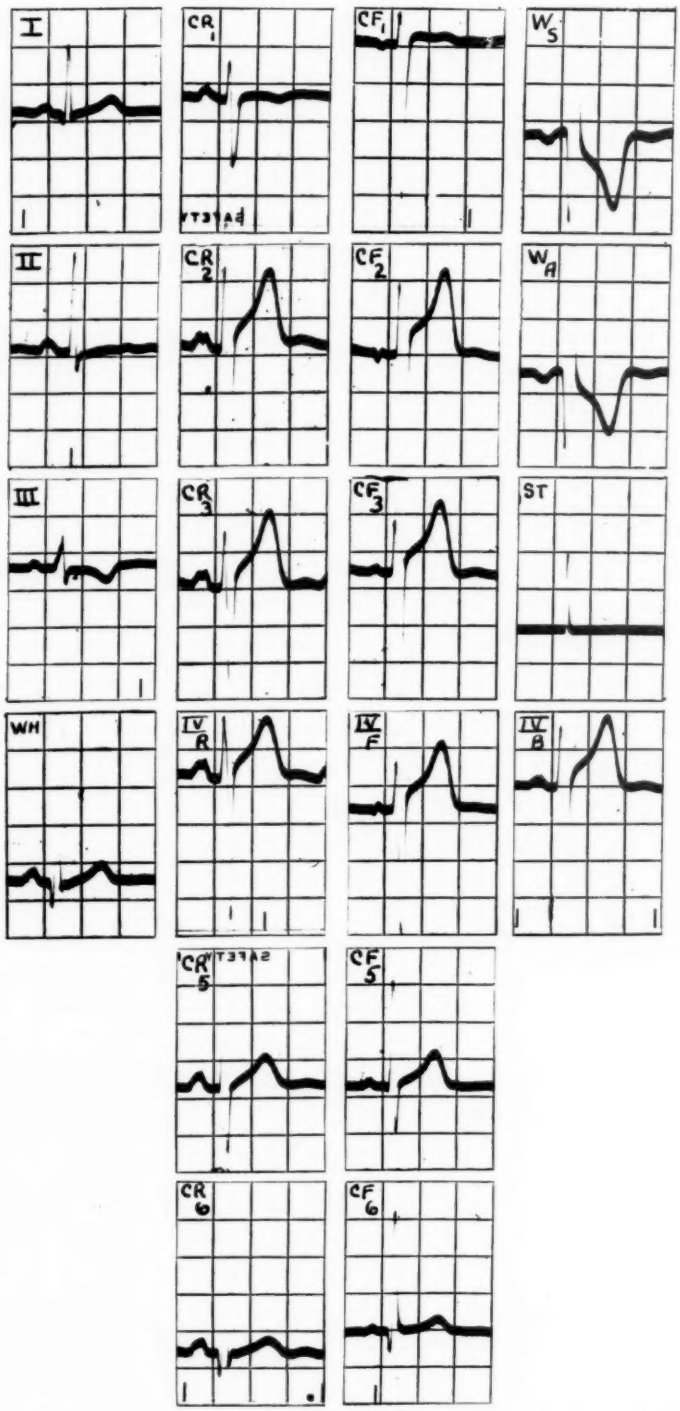



Fig. 11.—Electrocardiogram of a normal man. Observe that the T wave is diphasic in Lead II, and that, in Lead III, it is frankly inverted, with an S-T segment simulating a "cove-plane" contour. Note the notching of the P waves, which is most marked in Lead $CR_2$. The so-called Q wave in the Wolferth leads is smaller at the apex (WA) than in the parasternal (WS) position. Usually, the opposite is true.

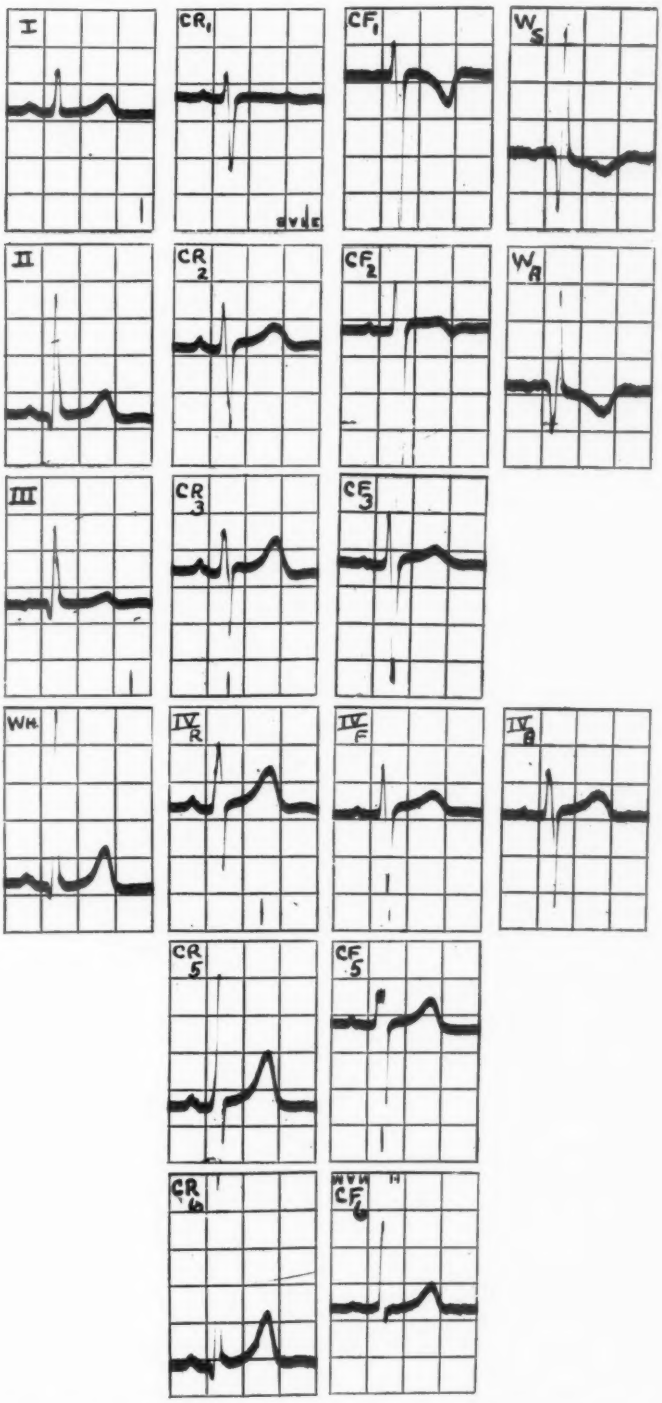



Fig. 12.—Electrocardiogram of a normal woman. Lead $CF_2$ illustrates the closest approach to an inverted T wave at position 2 which was encountered in the entire series.

TABLE

MAXIMAL AND MINIMAL MEASUREMENTS OF THE VARIOUS DEFLECTIONS IN THE STANDARD

| LEAD | P WAVE | | | | Q WAVE | | R WAVE | |
|---|---|---|---|---|---|---|---|---|
| | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL NEGATIVE DEFLECTION | MINIMAL NEGATIVE DEFLECTION | MAXIMAL DEFLECTION | MINIMAL DEFLECTION | MAXIMAL DEFLECTION | MINIMAL DEFLECTION |
| I | 0.9 | 0.2 | | | −0.9 | −0.1 | +12.20 | +2.40 |
| II | 2.0 | 0.2 | | | −1.8 | −0.1 | +23.6 | +4.3 |
| III | 1.8 | 0.2 | −0.5 | −0.1 | −3.4 | −0.1 | +19.1 | +1.3 |
| $CR_1$ | 2.1 | 0.2 | −0.3# | | 0.0 | 0.0 | +21.6 | +1.3 |
| $CR_2$ | 2.1 | 0.4 | | | 0.0 | 0.0 | +23.8 | +0.7 |
| $CR_3$ | 2.0 | 0.4 | | | −0.2# | | +29.0 | +1.1 |
| IVR | 1.8 | 0.7 | | | −1.0 | −0.2 | +35.+ | +6.3 |
| $CR_5$ | 2.0 | 0.7 | | | −1.7 | −0.1 | +35.+ | +13.2 |
| $CR_6$ | 1.8 | 0.5 | | | −2.6 | −0.1 | +35.+ | +8.1 |
| $CF_1$ | 0.5 | 0.2 | −1.7 | −0.2 | 0.0 | 0.0 | + 9.8 | +0.2 |
| $CF_2$ | 1.1 | 0.1 | −1.3 | −0.2 | 0.0 | 0.0 | +16.8 | +1.1 |
| $CF_3$ | 1.1 | 0.1 | −1.3 | −0.2 | −1.6 | −1.0 | +18.7 | +1.3 |
| IVF | 1.1 | 0.2 | −1.2 | −0.1 | −1.7 | −0.4 | +30.8 | +2.8 |
| $CF_5$ | 1.3 | 0.2 | −0.9 | −0.2 | −3.0 | −0.1 | +35.+ | +4.7 |
| $CF_6$ | 1.3 | 0.2 | −0.8 | −0.2 | −2.4 | −0.1 | +26.0 | +3.2 |
| Wolferth standard | 1.3 | 0.2 | | | 0.0 | 0.0 | −23.1 | −1.0 |
| Wolferth apex | 1.3 | 0.2 | | | +0.3# | | −35.+ | −5.2 |
| IVB | 1.3 | 0.2 | | | +0.1# | | +35.+ | +5.5 |
| Whitten | 1.4 | 0.4 | | | −3.2 | −0.1 | +35.+ | +11.8 |

*The T wave of one subject was directed downward in Lead II and had a depth of 1.3 mm. The maximal depth of negative T waves in Lead III, encountered in this group, was 2 mm., and the minimal depth, 0.5 mm. The T wave of one subject in Lead $CR_1$ was negative and measured 0.4 mm. The maximal depth of negative T waves in Lead $CR_3$, encountered in this group, was 6.0 mm., and the minimal depth, 0.2 mm. The maximal depth of downwardly directed T waves in the Wolferth standard lead was 15.1 mm., and the minimal depth, 1.7 mm. The corresponding maximal and minimal values for the downwardly directed T waves in the Wolferth apex lead were 15.0 mm. and 1.9 mm., respectively. The sign # indicates that the wave behaved that way in only one instance.

*The S-T Segment.*—In the precordial leads, the S-T segment usually arises above the isoelectric line, but it may arise at or even below it. The take-off varies from lead to lead, as indicated in the tables.

*The P-R Interval.*—The P-R interval ranged from 0.12 to 0.20 second. The averages for each lead are indicated in the tables.

*The QRS Complex.*—The duration of QRS varied from 0.06 to 0.12 second. The woman whose QRS time was consistently 0.12 second is a fine athlete, and her cardiac function is excellent even during very strenuous exertion. Notching and slurring of the QRS complexes were so common in both standard and precordial leads that no significance could be attached to them. The so-called "W" type of QRS complex was seen in Lead III six times (two men and four women), and the "M" type of QRS complex was encountered once, in a man (Lead III).

*Axis Deviation.*—Frank, marked, right axis deviation was not seen, although four men and four women exhibited slight right axis deviation. Left axis deviation was present and mild in eight men, very definite in two, and quite marked in one. Four women exhibited slight left axis deviation, and two showed only a moderate amount.

V

ELECTROCARDIOGRAMS AND PRECORDIAL LEADS OF FIFTY NORMAL ADULT MALES*

| S WAVE | | T WAVE | | S-T FROM P-R | | | | S-T FROM T-P | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| MAXIMAL DEFLECTION | MINIMAL DEFLECTION | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL NEGATIVE DEFLECTION | MINIMAL NEGATIVE DEFLECTION | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL NEGATIVE DEFLECTION | MINIMAL NEGATIVE DEFLECTION |
| - 6.7 | -0.2 | 4.3 | 0.4 | 0.9 | 0.0 | 0.3 | 0.0 | 0.8 | 0.0 | 0.5 | 0.0 |
| - 9.2 | -0.2 | 6.6 | 1.0 | 1.0 | 0.0 | 1.0 | 0.0 | 1.0 | 0.0 | 1.9 | 0.0 |
| - 7.5 | -0.1 | 2.6 | 0.3 | 0.8 | 0.0 | 0.6 | 0.0 | 1.0 | 0.0 | 1.3 | 0.0 |
| -22.9 | -2.2 | 9.9 | 0.4 | 2.0 | +0.2 | | | 1.7 | 0.0 | 0.1 | 0.0 |
| -31.0 | -4.5 | 15.3 | 3.2 | 4.0 | 0.9 | | | 3.9 | 0.4 | 0.3# | |
| -30.9 | -4.6 | 16.8 | 1.8 | 4.0 | 0.5 | | | 3.4 | 0.0 | | |
| -31.4 | -0.6 | 17.2 | 1.7 | 3.5 | 0.0 | | | 3.3 | 0.0 | 0.4 | 0.0 |
| -24.6 | -0.6 | 16.3 | 1.6 | 2.7 | 0.0 | 0.4# | | 2.0 | 0.0 | 0.6 | 0.0 |
| -13.8 | -0.6 | 14.0 | 0.7 | 2.0 | 0.0 | 0.4 | 0.0 | 1.4 | 0.0 | 1.0 | 0.0 |
| -35. + | -6.6 | 6.7 | 0.2 | 1.7 | 0.0 | 0.5 | 0.0 | 2.0 | 0.0 | 0.2 | 0.0 |
| -35. + | -7.0 | 15.5 | 3.1 | 3.5 | 0.2 | | | 3.5 | 0.4 | | |
| -35. + | -6.5 | 14.9 | 2.8 | 3.4 | 0.5 | | | 3.5 | 0.6 | | |
| -35. + | -1.4 | 14.3 | 0.8 | 3.0 | 0.3 | 0.2# | | 3.0 | 0.0 | | |
| -22.0 | -1.8 | 12.3 | 0.7 | 2.0 | 0.0 | 1.3 | 0.0 | 2.2 | 0.0 | 1.3 | 0.0 |
| - 7.6 | -0.1 | 9.6 | 0.4 | 1.0 | 0.0 | 0.6 | 0.0 | 1.0 | 0.0 | 0.4 | 0.0 |
| +35. + | +4.6 | | | | | 4.0 | 0.3 | | | 3.8 | 0.0 |
| +34.0 | +0.6 | | | | | 3.5 | 0.2 | | | 3.3 | 0.1 |
| -33.0 | -0.5 | 15.2 | 1.8 | 3.5 | +0.1 | | | 3.4 | 0.1 | | |
| -10.8 | -0.3 | 10.9 | 1.6 | 1.4 | 0.0 | -1.5 | 0.0 | 1.0 | 0.0 | 1.6 | 0.0 |

## CONCLUSIONS

A conductive electrode paste is necessary in order to obtain satisfactory precordial leads.

CR leads appear to be better than CL leads, which, in turn, are better than CF leads, for the following reasons:

1. CR and CL leads are obtained more conveniently than CF leads. After the three standard leads are derived, CR and CL leads can be taken with the shifting of only one lead wire; obtaining the CF lead necessitates shifting two lead wires.

2. The P wave in CR leads is usually upright. It is almost as frequently upright in CL leads. It is usually diphasic or inverted in CF leads.

3. Usually, the R wave in Lead IVR exceeds the value of R in Lead IVF. Compare the minimal value of the R wave in fifty normal males (Table V) in Lead IVR (+6.3 mm.) with the minimal value for R in IVF (+ 2.8 mm.). Inasmuch as diminution, rather than absence, of the R wave in these leads will constitute a part of the diagnostic criteria in the appraisal of cardiac disease, it is important that the minimal value of R be not too small. Moreover, it will be seen that, in both men and women, the amplitude of the R wave is maintained much better in Leads $CR_5$ and $CR_6$ than in Leads $CF_5$ and $CF_6$. In women, minimal values

TABLE

MAXIMAL AND MINIMAL MEASUREMENTS OF THE VARIOUS DEFLECTIONS IN THE STANDARD

| LEAD | P WAVE | | | | Q WAVE | | R WAVE | |
|---|---|---|---|---|---|---|---|---|
| | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL NEGATIVE DEFLECTION | MINIMAL NEGATIVE DEFLECTION | MAXIMAL DEFLECTION | MINIMAL DEFLECTION | MAXIMAL DEFLECTION | MINIMAL DEFLECTION |
| I | 1.1 | 0.2 | | | −0.6 | −0.1 | +11.5 | +1.2 |
| II | 2.6 | 0.4 | | | −0.7 | −0.1 | +21.0 | +1.5 |
| III | 1.8 | 0.2 | | | −4.6 | −0.1 | +17.3 | +1.1 |
| $CR_1$ | 2.2 | 0.3 | | | 0.0 | 0.0 | +8.1 | +0.1 |
| $CR_2$ | 2.7 | 0.3 | | | 0.0 | 0.0 | +13.6 | +0.6 |
| $CR_3$ | 2.4 | 0.4 | | | 0.0 | 0.0 | +17.1 | +0.9 |
| IVR | 2.4 | 0.5 | | | 0.0 | 0.0 | +35. + | +1.1 |
| $CR_5$ | 2.3 | 0.4 | | | −1.1 | −0.1 | +35. + | +7.3 |
| $CR_6$ | 2.1 | 0.4 | 0.6# | | −1.8 | −0.1 | +35. + | +7.6 |
| $CF_1$ | 0.3# | | −2.0 | −0.2 | 0.0 | 0.0 | + 6.5 | +0.2 |
| $CF_2$ | 2.6 | 0.3 | −1.7 | −0.1 | 0.0 | 0.0 | +10.7 | +0.2 |
| $CF_3$ | 0.6 | 0.2 | −1.4 | −0.1 | 0.0 | 0.0 | +13.0 | +1.6 |
| IVF | 0.6 | 0.3 | −1.1 | −0.2 | 0.0 | 0.0 | +39.0 | +1.2 |
| $CF_5$ | 0.6 | 0.2 | −0.9 | −0.2 | −1.0 | −0.1 | +24.9 | +1.8 |
| $CF_6$ | 1.8 | 0.2 | −0.4 | −0.1 | −1.4 | −0.1 | +30.4 | +1.0 |
| Wolferth standard | 0.0 | 0.0 | −1.2 | −0.2 | 0.0 | 0.0 | −11.6 | −1.4 |
| Wolferth apex | 0.1 | 0.0 | −1.0 | −0.2 | 0.0 | 0.0 | −35.4 | −1.4 |
| IVB | 1.0 | 0.1 | | | 0.0 | 0.0 | +37.3 | +1.8 |
| Whitten | 1.8 | 0.1 | | | −2.1 | −0.1 | +31.6 | +6.7 |

*The maximal depth of negative T waves in Lead III, encountered in this group, was 1.6 mm., and the minimal depth 0.4 mm. The corresponding values of negative T waves in Lead $CF_1$ were 3.9 mm. and 0.3 mm. respectively. The maximal depth of downwardly directed T waves in the Wolferth standard lead was 7.5 mm., and the minimal depth, 1.6 mm. The corresponding maximal and minimal values for the downwardly directed T waves in the Wolferth apex lead were 11.2 mm. and 1.8 mm., respectively. The sign # indicates that the wave behaved that way in only one instance. The "pathologic," upright T wave in the Wolferth standard lead was not present in a recheck series.

of the R wave are approximately the same in Leads IVR and IVF. In women, minimal values of the S wave in Leads IVR and IVF are essentially the same.

4. The T wave has a greater amplitude in Lead IVR (average +8.8 mm. in both sexes; minimal +1.7 mm. in men) than it has in Lead IVF (average +6.2 mm. in both sexes; minimal +0.8 mm. in men). Inasmuch as it will be necessary to evaluate low voltage of the T waves in these leads in the diagnosis of cardiac disease, it is desirable that the minimal values be not too low. Similarly, the amplitude of the T wave in Leads $CR_5$ and $CR_6$ is maintained better than it is in Leads $CF_5$ and $CF_6$.

5. In one instance, the T wave approached negativity in Lead $CF_2$. This never occurred in Lead $CR_2$.

6. CR and CL leads frequently, but not constantly, exhibit lesser degrees of deviation of the S-T segments from the level of the P-R and T-P segments than do CF leads.

7. In technical studies such as this, the importance of a perfectly level base line cannot be overemphasized. It was observed throughout this study that during the taking of CR, CL, and CF leads at a given

VI

ELECTROCARDIOGRAMS AND PRECORDIAL LEADS OF FIFTY NORMAL ADULT FEMALES*

| S WAVE | | T WAVE | | S-T FROM P-R | | | | S-T FROM T-P | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| MAXIMAL DEFLECTION | MINIMAL DEFLECTION | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL NEGATIVE DEFLECTION | MINIMAL NEGATIVE DEFLECTION | MAXIMAL POSITIVE DEFLECTION | MINIMAL POSITIVE DEFLECTION | MAXIMAL NEGATIVE DEFLECTION | MINIMAL NEGATIVE DEFLECTION |
| −3.0 | − 0.1 | 3.6 | 0.4 | 0.8 | 0.0 | 0.2 | 0.0 | 0.1 | 0.0 | 0.5 | 0.0 |
| −5.2 | − 0.1 | 4.7 | 0.3 | 0.5 | 0.0 | 0.8 | 0.0 | 0.1 | 0.0 | 1.9 | 0.0 |
| −5.0 | − 0.1 | 2.4 | 0.2 | 0.4 | 0.0 | 1.0 | 0.0 | 0.3 | 0.0 | 1.5 | 0.0 |
| −16.0 | − 3.8 | 4.6 | 0.1 | 1.4 | 0.0 | | | 0.9 | 0.0 | 1.0 | 0.0 |
| −26.3 | − 6.6 | 12.1 | 2.3 | 2.6 | 0.1 | | | 2.1 | 0.0 | 0.6 | 0.0 |
| −29.6 | − 4.9 | 11.8 | 2.6 | 2.1 | 0.2 | | | 1.6 | 0.0 | 0.4 | 0.0 |
| −21.7 | − 2.1 | 13.6 | 2.6 | 2.3 | 0.0 | 0.1 | 0.0 | 1.8 | 0.0 | 1.1 | 0.0 |
| −15.1 | − 0.4 | 13.0 | 2.0 | 1.4 | 0.0 | 1.2 | 0.0 | 1.0 | 0.0 | 1.5 | 0.0 |
| − 7.1 | − 0.4 | 10.7 | 1.6 | 0.9 | 0.0 | 1.3 | 0.0 | 0.9 | 0.0 | 2.2 | 0.0 |
| −33.4 | − 6.7 | 3.9 | 0.3 | 1.3 | 0.0 | 0.1 | 0.0 | 1.7 | 0.0 | 0.3 | 0.0 |
| −35.+ | −12.0 | 10.1 | 1.7 | 2.4 | 0.0 | | | 2.5 | 0.0 | 0.2 | 0.0 |
| −35.+ | − 8.1 | 9.3 | 1.2 | 2.5 | 0.0 | | | 2.4 | 0.0 | 0.2 | 0.0 |
| −27.3 | − 2.2 | 9.3 | 1.3 | 2.6 | 0.0 | | | 2.0 | 0.2 | 0.2 | −0.1 |
| −18.9 | − 8.6 | 8.9 | 1.2 | 1.4 | 0.0 | 0.8 | 0.0 | 1.4 | 0.0 | 1.2 | −0.0 |
| − 8.9 | − 0.1 | 6.1 | 0.6 | 0.7 | 0.0 | 0.7 | 0.0 | 1.0 | 0.0 | 0.9 | 0.0 |
| +28.0 | + 8.1 | 1.1# | | | | 2.2 | 0.0 | 0.2 | 0.0 | 2.0 | 0.0 |
| +33.2 | + 4.6 | | | | | 2.2 | 0.0 | 0.1 | 0.0 | 2.0 | 0.0 |
| −33.2 | − 5.2 | 11.8 | 1.9 | 2.4 | 0.0 | | | 1.9 | 0.1 | 0.2 | 0.1 |
| − 4.9 | − 0.1 | 7.8 | 1.3 | 0.6 | 0.0 | −0.6 | 0.0 | 0.4 | 0.0 | 1.1 | 0.0 |

position, it was frequently more difficult to achieve a perfectly level base line when the left leg was the indifferent electrode (CF leads) than when either arm was used (CR or CL leads).

The range of normal for the various deflections varies with the position of the indifferent electrode and with the sex of the subject. Therefore, the separate standards of normal variability established for each sex by this study are of vital importance when the presence or absence of abnormality is being considered. Of the quantitative determinations made on multiple chest lead electrocardiograms obtained from one hundred normal adults (fifty men and fifty women), the following have particular clinical significance: Minimal values of the R wave in Leads IVR and IVF for men are +6.3 and +2.8 mm., respectively; corresponding values for women are +1.1 and +1.2 mm., respectively. Minimal values of the S wave in Leads IVR and IVF for men are −0.6 and −1.4 mm., respectively; corresponding values for women are −2.1 and −1.2 mm., respectively. The minimal height of the T wave in Leads IVR and IVF for men is +1.7 and +0.8 mm., respectively; corresponding values for women are +2.6 and +1.3 mm., respectively.

REFERENCES

1. Wolferth, C. C., and Wood, F. C.: The Electrocardiographic Diagnosis of Coronary Occlusion by the Use of Chest Leads, Am. J. M. Sc. **183**: 30, 1932.
2. Master, A. H.: The Precordial Lead in 104 Normal Adults, AM. HEART J. **9**: 511, 1934.

3. Shipley, R. A., and Hallaran, W. R.: The Four-Lead Electrocardiogram in Two Hundred Normal Men and Women, AM. HEART J. **11**: 325, 1936.
4. Sorsky, Eliot, and Wood, Paul: The Use of Chest Leads in Clinical Electrocardiography. I. Normal Variations, AM. HEART J. **13**: 183, 1937.
5. Master, A. M., Dack, S., and Jaffe, H. L.: Chest Leads in Normal Children, Proc. Soc. Exper. Biol. & Med. **32**: 1529, 1935.
6. Rosenblum, Harold, and Sampson, J. J.: A Study of Lead IV of the Electrocardiogram in Children With Especial Reference to the Direction of the Excursion of the T Wave, AM. HEART J. **11**: 49, 1936.
7. Special Article: Standardization of Precordial Leads. Joint Recommendations of the American Heart Association and The Cardiac Society of Great Britain and Ireland, AM. HEART J. **15**: 107, 1938; supplementary report **15**: 235, 1938.
8. Standardization of Precordial Leads (Miscellany), J. A. M. A. **110**: 395, 1938; supplementary report **110**: 681, 1938.
9. Whitten, M. B.: Midaxillary Leads of the Electrocardiogram in Myocardial Infarction, AM. HEART J. **13**: 701, 1937.

# PHONOCARDIOGRAPHIC STUDIES OF EARLY RHEUMATIC MITRAL DISEASE

ALBERTO C. TAQUINI, M.D., BUENOS AIRES, ARGENTINA,
BENEDICT F. MASSELL, M.D., AND BERNARD J. WALSH, M.D.,
BOSTON, MASS.

THE studies which form the basis of the present report were performed in an attempt to elucidate the physiologic mechanism of certain auscultatory signs which are associated with early rheumatic mitral disease. At the House of the Good Samaritan, where we have had an opportunity to observe a large number of children during the first year of their rheumatic fever, it has been our experience that the physical signs of early involvement of the mitral valve show the following characteristics:

There is always an apical systolic murmur, which is of at least moderate intensity and is constant. The murmur sometimes begins with a definite first heart sound. Often the first sound is completely or partly masked, so that the onset of ventricular systole is marked by the beginning of the murmur. Although diastole may be entirely silent, an extra, or third, sound in the early part of diastole, or a diastolic murmur, is frequently heard. The diastolic murmur is often discrete, and starts with a third sound or at about the time in diastole when a third sound would normally occur.

Occasionally, the diastolic murmur seems to be hardly more than a slightly prolonged third sound, so that its exact differentiation from the latter may be difficult.

Third sounds and discrete diastolic murmurs are heard more often when the patient has little or no cardiac enlargement, and a mild or quiescent rheumatic infection. When the disease is more severe, with tachycardia and, usually, moderate to marked cardiac enlargement, the diastolic murmur is more likely to be a poorly defined rumble of low intensity. A few severely ill patients, with rapid heart rates (140-150), have an apparent presystolic murmur which, however, lacks the crescendo quality associated only with definite mitral stenosis. Rarely, this murmur is accompanied by a thrill.

Since it is generally accepted that the systolic murmur which is associated with disease of the mitral valve is caused by mitral regurgitation, we have confined our studies to the sounds and murmurs occurring during diastole. That the diastolic murmur, or rumble, of early rheumatic mitral involvement is seldom indicative of anatomic mitral stenosis was pointed out by Bland, White, and Jones,[1] who found that patients who died of rheumatic fever within one year of its onset rarely, if ever, had any narrowing, or even appreciable deformity, of the mitral valve.

From the House of the Good Samaritan, Boston, Mass.
Received for publication Dec. 11, 1939.

They suggested that the murmur might be caused, in these special instances, either by a "relative stenosis of the orifice in relation to the dilated ventricular cavity," or by "vibrations set up by the diastolic filling of a capacious cavity with relaxed and relatively atonic walls."

It seemed to us that a better understanding of the mechanism of these diastolic sounds might be obtained by recording and correlating them with various other events in the cardiac cycle. Therefore, phonocardiograms were taken synchronously with electrocardiograms, or tracings of the venous pulse, or apical pulsations. An electrical method was used exclusively.*

Studies were made of fifteen unselected patients with mitral involvement who had been ill with rheumatic infection for less than one year. Their ages varied from four to twelve years. In each instance the phonocardiograms were taken after the results of a careful clinical examination had been recorded.

These patients may be divided into three groups, according to the auscultatory signs at the mitral area: (1) Five patients had a systolic murmur and a definite, extra heart sound early in diastole. In all of these cases the rheumatic infection had become either quiescent or low-grade. Their hearts were either normal in size or only slightly enlarged. (2) Nine patients had a systolic murmur and a definite diastolic rumble (without a presystolic crescendo phase). The first three of this group had only a low-grade rheumatic infection, and hearts which were either normal in size or slightly enlarged. The remaining six patients were moderately to severely ill, and their hearts were moderately to greatly enlarged. (3) One patient had a systolic and a presystolic murmur; the latter had no crescendo quality, but was accompanied by a thrill. This patient was extremely ill, and had a very large heart.

## PHONOCARDIOGRAPHIC OBSERVATIONS

The phonocardiograms of the five patients in the first group showed a first heart sound, followed by a systolic murmur, a second heart sound, and, in diastole, an extra sound. In three of the five patients this extra sound occurred during the fall of the V wave of the venous pulse. This time relation indicated that the extra sound was a normal third heart sound.[2, 3, 4] In the remaining two patients of the first group, the vibrations composing the extra sound were similar in appearance to those in the previous records, except that they occurred at a shorter interval after the second sound, and synchronously with the apex of the V wave of the venous pulse (Fig. 1). This suggests that the extra sound in these two cases might have been caused by the opening snap of the mitral valve, and therefore was not a real third heart sound. However, it has been shown that the isometric relaxation phase of the left ventricle may be shortened when there is mitral regurgitation.[5] Under such circumstances, the third sound, which is produced during rapid

*All of the tracings which were made in this investigation were registered by electrical mechanisms and their associated optical systems. The Sanborn Stetho-Cardiette which was employed contains two electrical recording systems. One of the systems is especially suited to the graphic registration of heart sounds. The second system is designed specifically to record the electrocardiogram. A special type of crystal microphone is employed to convert the pressure variations of the venous pulse or apical beat into corresponding electrical impulses, which are then recorded by the cardiograph portion of the Stetho-Cardiette.

inflow into the left ventricle, might not show its usual relation to the V wave of the venous pulse, for the latter is associated with pressure changes in the right ventricle. Therefore, in order to ascertain the nature of the extra sound in these cases, it was necessary to take phonocardiograms simultaneously with records of the apical pulsation. In both cases the extra sound occurred synchronously with the phase of rapid inflow into the left ventricle, which is indicated by the R. I. peak* in the apical pulse tracing (Fig. 2). We have concluded, therefore, that, in these two cases, as well as in the previous ones, the extra sound was a real third heart sound.

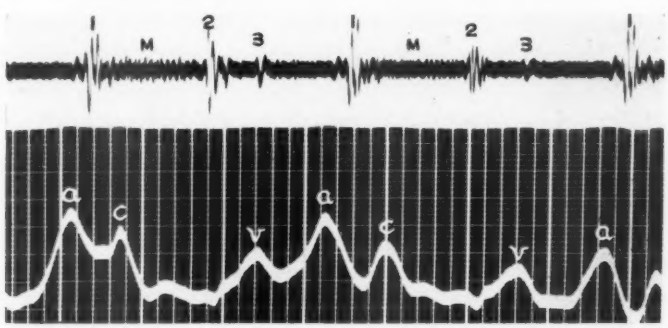



Fig. 1.—Simultaneously recorded phonocardiogram and venous pulse. The third sound appears synchronously with the apex of the V wave.

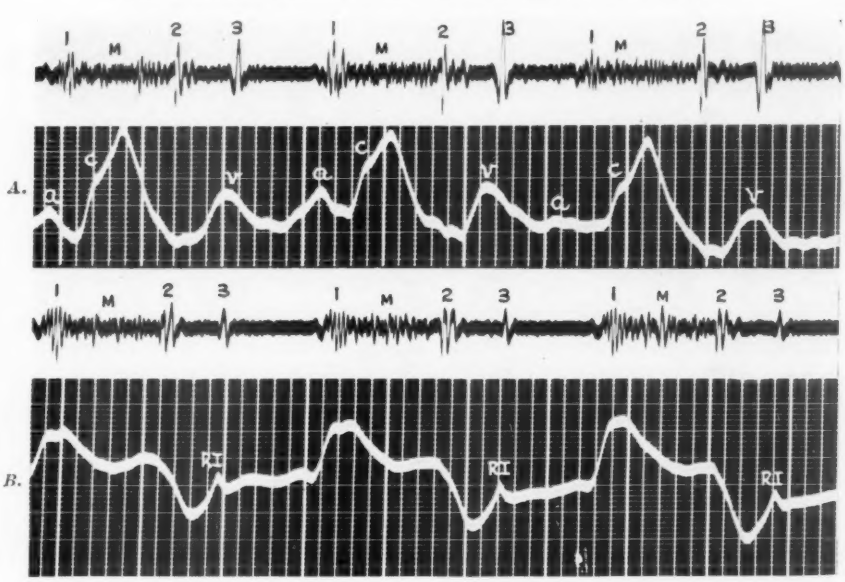



Fig. 2.—*A*, simultaneously recorded phonocardiogram and venous pulse. The third sound appears synchronously with the apex of the V wave. *B*, simultaneously recorded phonocardiogram and apical pulse in the same patient. The third sound appears synchronously with rapid inflow (R. I.) into the left ventricle.

*This wave has been referred to as "the protodiastolic wave" by Bridgman,[6] and "the rapid positive wave" by Orías and Braun-Menéndez.[4]

In some of the cases the phonocardiographic records showed vibrations which occurred about 0.10 second after the beginning of the P wave of the electrocardiogram. It is likely that they represent auricular sounds, in spite of the fact that they were inaudible (Fig. 3).

The phonocardiograms of the second group of nine patients (those with both systolic and diastolic murmurs by auscultation) were not entirely alike. All showed the first sound, followed by a systolic murmur and a second sound, but the graphic phenomena during diastole were variable, and the variation apparently depended on the length of diastole.

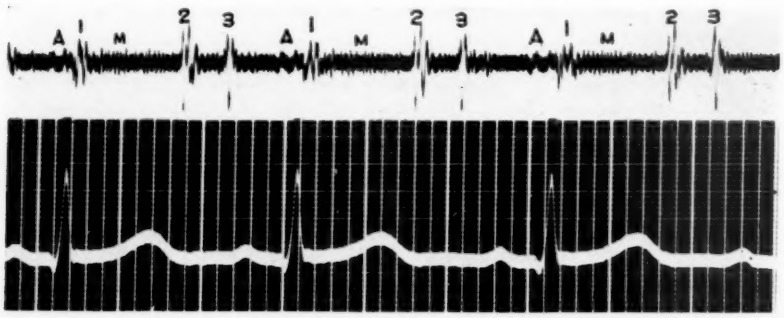



Fig. 3.—Simultaneously recorded phonocardiogram and electrocardiogram. A group of vibrations (*A*) appears about 0.10 second after the beginning of the P wave.

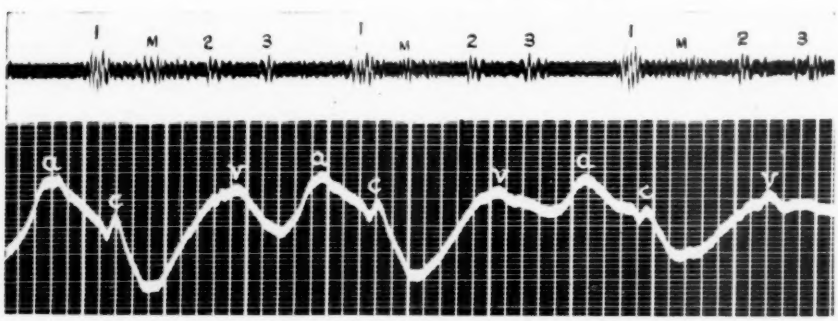



Fig. 4.—Simultaneously recorded phonocardiogram and electrocardiogram. A group of vibrations (*J*) occurs synchronously with the fall of the V wave.

The phonocardiograms of the first patient, whose heart rate was relatively slow (under 100), showed one group of oscillations during diastole. These occurred during the fall of the V wave of the venous pulse and were synchronous with the R. I. peak of the apical pulsation, and therefore coincided with the phase of rapid inflow. It is apparent that these vibrations occupied the same location in diastole as the normal third sound. Furthermore, the appearance of these vibrations was similar to that of the third sound in the phonocardiograms of the first group of patients, except that they were of slightly longer duration. (The simultaneously recorded phonocardiogram and venous pulse tracing are shown in Fig. 4.)

The next two patients had slightly more rapid heart rates (about 100). Their phonocardiograms showed, in diastole, two groups of vibrations. The first set of vibrations, as in the previous case, was a prolonged third sound. The second group of vibrations, which followed the first by a very short interval, occurred about 0.10 second after the beginning of the P wave of the electrocardiogram. This sound, which was produced during auricular systole, had the same time relations and phonocardiographic characteristics as the auricular sound (see Fig. 5).

In these phonocardiograms, the presence or absence of vibrations caused by auricular systole was related to the length of diastole. When diastole was relatively long, the vibrations were very small or did not appear, because most of the blood had already passed from the auricle into the ventricle before auricular systole occurred. When diastole was shorter, sufficient blood remained in the auricle to be expelled forcibly into the ventricle by auricular systole. This resulted in further distention of the ventricular walls and produced larger auricular sound vibrations.*

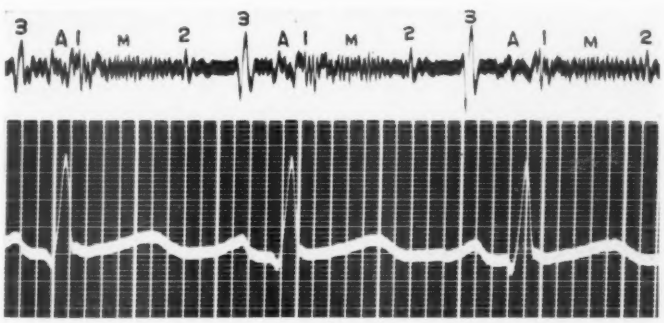



Fig. 5.—Simultaneously recorded phonocardiogram and electrocardiogram. There are two groups of vibrations in diastole, one caused by the third sound (*3*), the other by the auricular sound (*A*).

There were five patients with tachycardia (about 130) whose phonocardiograms showed only one group of oscillations during diastole, and these were of relatively large amplitude (Fig. 6). Phonocardiograms which were taken simultaneously with the venous pulse or apical pulsation showed that in these cases, in which diastole was shortened, rapid inflow and auricular systole occurred at the same moment. (The simultaneously recorded phonocardiogram and venous pulse in one of these cases is shown in Fig. 7.) It is therefore likely that in these patients the single large group of oscillations was the result of ventricular distention produced by the combined effect of rapid inflow and auricular systole.

Further evidence that this interpretation is correct is presented by the record of a patient who had sinus arrhythmia and a prolonged

*It has been shown that that portion of the auricular sound which can be recorded from the precordial area is caused by vibrations set up in the ventricular walls by the impact of the blood which is forced into the ventricle by auricular contraction.[7]

auriculoventricular conduction time (Fig. 8). It is apparent that, depending on the duration of diastole, there are (1) two definitely separate groups of vibrations, (2) a single but prolonged vibration period with one group of vibrations immediately following the other, or (3) a shorter period of somewhat larger vibrations caused by superimposition of one group on the other.

Thus it appears that the diastolic rumble in these nine patients with early rheumatic mitral disease corresponded to (a) one group of vibrations which, phonocardiographically, was a prolonged third sound, (b) two successive, but separate, groups of vibrations, the first of which occurred when the ventricle was being distended by rapid inflow during early diastole, and was therefore a prolonged third sound, and the second when the ventricle was distended by auricular systole, and was therefore an auricular sound, or (c) one large group of vibrations caused by summation of the oscillations of the third and auricular sounds.

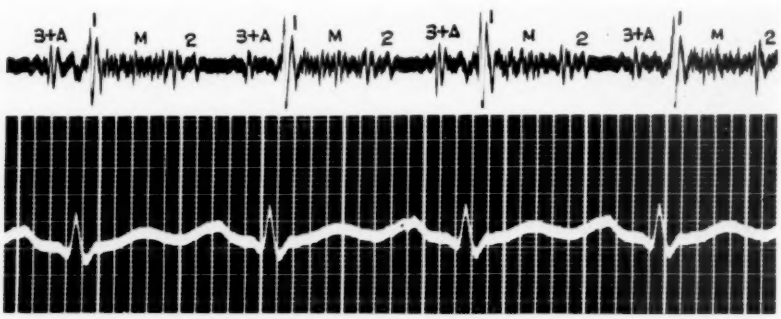



Fig. 6.—Simultaneously recorded phonocardiogram and electrocardiogram. In diastole there appears one large group of vibrations about 0.10 second after the beginning of the P wave. This is produced by the combined third (*3*) and auricular (*A*) sounds.

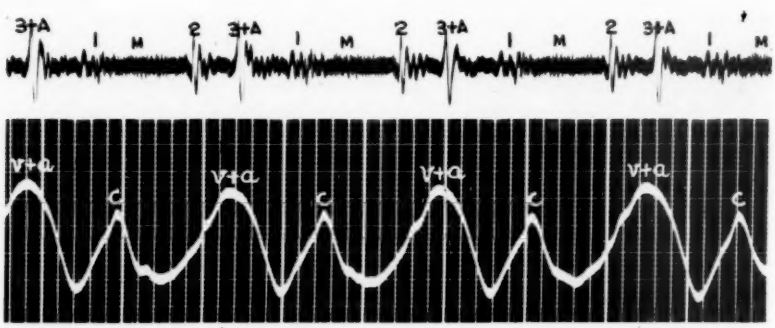



Fig. 7.—Simultaneously recorded phonocardiogram and venous pulse. The venous pulse shows a summation of the V and A waves. The phonocardiogram shows one large group of vibrations in diastole which represents a combination of the third (*3*) and auricular (*A*) sounds.

One patient in the third clinical group was separated from the others because his diastolic murmur seemed to be presystolic in time and was

accompanied by a thrill. However, phonocardiograms which were taken simultaneously with the venous pulse or apical pulsation showed that, as in the previous patients, the diastolic vibrations were caused by combined third and auricular sounds.

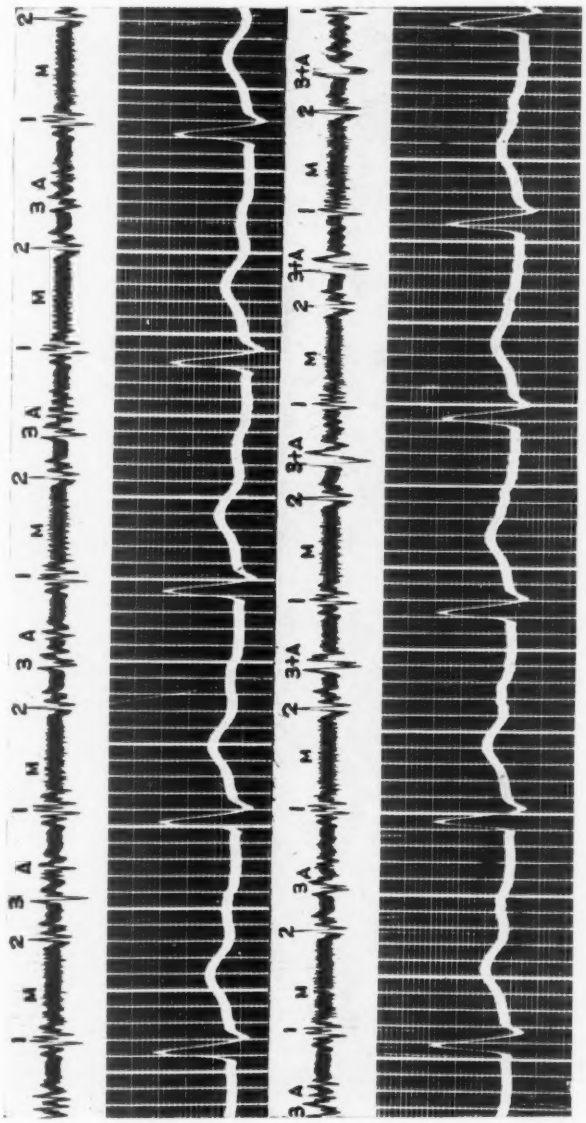


Fig. 8.—Simultaneously recorded phonocardiogram and electrocardiogram (the upper and lower records are continuous). The record shows the auricular sound either (*A*) definitely separated from the third sound (*3*), immediately after the third sound, or superimposed upon the third sound, depending upon the duration of diastole.

## DISCUSSION AND CONCLUSIONS

These phonocardiographic studies show that the third sound, which is commonly present in normal children, is unusually prominent in some patients with early rheumatic mitral disease, and may even be

sufficiently prolonged to produce a diastolic rumble. The frequent occurrence of the third sound in normal children may be explained by their relatively thin ventricular and chest walls. The unusual prominence of the third sound, and its frequent prolongation into a rumble, in patients with early rheumatic mitral disease may be related to two additional factors. The first is the effect of mitral regurgitation. This increases the amount of blood which flows into the left auricle, and thereby greatly augments the intra-auricular pressure. As a result, a larger amount of blood passes with increased force into the left ventricle during rapid inflow, and this produces a degree of distention of its walls which is greater than normal. The second factor may be a decreased tonicity of the ventricular musculature consequent to the rheumatic infection.

In patients with slightly increased heart rates, the presence of an audible auricular sound following quickly after a somewhat prolonged third sound enhances the auditory effect of a rumble.

When there is considerable tachycardia, auricular contraction may occur simultaneously with rapid inflow, so that their effects are combined. The resulting overdistention of the ventricle produces vibrations which represent superimposed third and auricular sounds. These relatively strong vibrations, together with a short diastole, again produce the acoustic effect of a rumble.

## SUMMARY

Clinical experience has shown that patients with rheumatic mitral valve involvement of less than one year's duration always have an apical systolic murmur of at least moderate intensity. In addition, they frequently have in diastole a moderately loud extra sound or a rumbling murmur.

Phonocardiograms were taken synchronously with electrocardiograms or tracings of the venous pulse or apical pulsations in fifteen unselected cases of early rheumatic mitral involvement. From these studies we have concluded that:

1. The audible extra sound appears, in the phonocardiogram, as a series of vibrations which occur at the moment when the left ventricle is distended by rapid inflow, and is therefore a real third sound.

2. In some cases, prolongation of the vibrations of the third sound may produce the acoustic effect of a rumble.

3. In other cases, the vibrations of the auricular sound which occur very shortly after, or are superimposed upon, prolonged vibrations of the third sound enhance the acoustic effect of a rumble.

We are grateful to Mr. Morris Rappaport, of the Sanborn Company, for technical assistance.

## REFERENCES

1. Bland, E. F., White, P. D., and Jones, T. D.: The Development of Mitral Stenosis in Young People, AM. HEART J. **10**: 995, 1935.
2. Thayer, W. K.: Further Observations on the Third Heart Sound, Arch. Int. Med. **4**: 297, 1909.
3. Wiggers, C. J.: Physiology in Health and Disease, Ed. 3, Philadelphia, 1939, p. 609, Lea & Febiger.
4. Orías, O., and Braun-Menéndez, E.: The Heart Sounds in Normal and Pathological Conditions, 1939, pp. 98-106, Oxford University Press.
5. Taquini, A. C.: Exploracion Del Corazon Por Via Isofagica, 1936, p. 87, El. Ateneo, Buenos Aires, Argentina.
6. Bridgman, E. W.: Observations on the Third Heart Sound, Heart **6**: 41, 1915-1917.
7. Orías, O., and Braun-Menéndez, E.: The Heart Sounds in Normal and Pathological Conditions, 1939, p. 120, Oxford University Press.

# RESPONSE TO RENIN OF UNANESTHETIZED NORMAL AND NEPHRECTOMIZED RATS*

ARTHUR FREEDMAN, M.D.
CINCINNATI, OHIO

IT WAS shown by Tigerstedt and Bergmann,[1] in 1898, that the pressor response of rabbits to renin was greater after the animals had been nephrectomized. It was further demonstrated by Merrill, Williams, and Harrison,[2] who worked with rats, that, by waiting two or three days after nephrectomy, both the degree and duration of the renin pressor effects were enhanced. All of these experiments were performed on anesthetized animals, however, and, since Shaw[3] believed that this factor influenced the renin effect, it seemed desirable to repeat the work of Merrill, Williams, and Harrison on unanesthetized animals.

## METHOD

Williams, Harrison, and Grollman's apparatus[4] was used for taking serial systolic pressure readings on rats at frequent intervals. Unanesthetized animals were trained to the routine and taught to remain quiet while their pressures were being taken. After control pressures were recorded, 1 c.c. of renin† was administered intraperitoneally. The rats' pressures were followed at one- or two-minute intervals for the first ten minutes, once or twice again during the first hour, and frequently during successive hours. Inasmuch as the method requires that the rats be warmed in order to produce adequate peripheral vasodilation, care was taken to establish a constant, slow heating time, and to avoid overheating.

The rats chosen were males, weighing from 230 to 280 Gm., and nonpregnant females which weighed 180 to 220 Gm.; ten normal and nine nephrectomized animals were used. Comparison of the same animal's response to renin before and after nephrectomy was made in several instances. Nephrectomy was performed under light ether anesthesia through flank incisions; the animals resumed their normal behavior within half an hour after operation. The animals responded but little, or not at all, to renin for the first few hours after nephrectomy, and it was therefore decided to wait a minimum of nine hours after operation before making the injections. Control pressures after nephrectomy were of the same order as those prior to operation, averaging 118 mm. of mercury in normal animals and 115 mm. in nephrectomized animals.

## RESULTS

As shown by the charts, nephrectomized animals differed decidedly from normal ones in their responses to renin. This was true of both the intensity and duration of the effect. The blood pressures of the normal animals rose an average of 30 mm. of mercury within from four

From the Department of Medicine, Vanderbilt University, Nashville, Tenn.
*This work was aided by a grant from the Josiah Macy, Jr., Foundation.
Received for publication Jan. 13, 1940.

†Renin was prepared from hog kidneys by a modification of the method of Grossman.[5] To the dried powder which remained after alcohol and ether extractions, there was added 1 c.c. of normal saline for each gram of original cortex. This was allowed to stand in the refrigerator for twenty-four hours and was then centrifuged. The supernatant fluid was a clear, reddish-brown liquid which possessed a rapid pressor action, with no initial depressor effect, when injected into the aortas of anesthetized rats, and when injected intraperitoneally into unanesthetized rats.

to seven minutes after the injection of renin; the highest rise was 44 mm. By contrast, the nephrectomized animals responded with an average rise, in the same period, of 58 mm.; one animal's blood pressure rose 108 mm. of mercury above its control level. The average, immediate, blood pressure rise of the nephrectomized rats was therefore almost twice that of the normals.

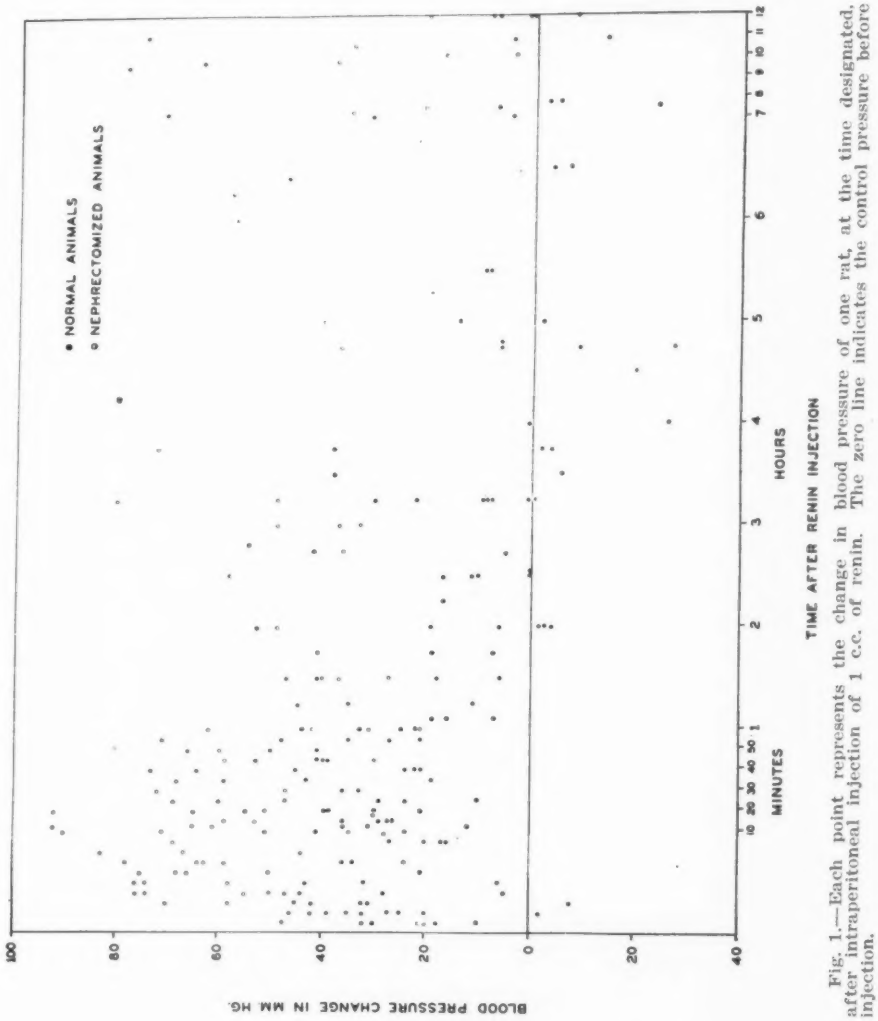



Fig. 1.—Each point represents the change in blood pressure of one rat, at the time designated, after intraperitoneal injection of 1 c.c. of renin. The zero line indicates the control pressure before injection.

After these prompt initial elevations, the pressures of the normal animals subsided to approximately preinjection levels within two or three hours, but the blood pressures of the nephrectomized animals did not return to normal levels in less than five hours, and frequently remained elevated for as long as twelve hours. Occasionally, an animal died twenty hours, or more, after the injection, with all recorded pres-

sures still above the control level. When an average was taken of the amount of blood pressure change during the period from four to twelve hours after nephrectomy, it was found that the pressures were still 39 mm. of mercury above the preinjection level. At this time the blood pressures of the rats with intact kidneys were almost normal.

## COMMENT

These observations indicate that the increased sensitivity of nephrectomized animals to renin, which has been observed by others,[1, 2] is not related to anesthesia. In fact, the opportunity for prolonged observation of the unanesthetized animal makes the increase in sensitivity seem more pronounced than that reported by Merrill, Williams, and Harrison.[2] The experiments suggest also that normal renal tissue may play some role with regard to the fate in the body of artificially administered renin. The fact that rats are inexpensive, and that there is a simple and direct method of measuring their blood pressure frequently, a method which enables one to measure the pressures of relatively large numbers of animals in a short period of time, makes their use for the assay of kidney extracts feasible.

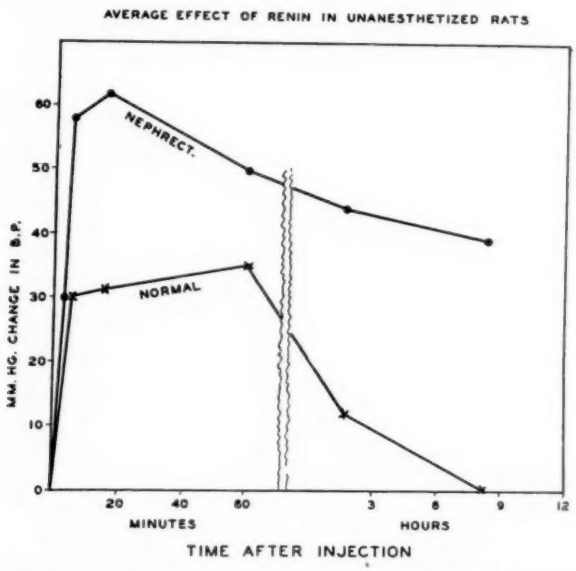



Fig. 2.—Composite curves, showing the average blood pressure change of all normal and all nephrectomized rats after intraperitoneal injection of 1 c.c. of renin. The base line represents the average pressure before injection. The first point is an average of all blood pressure readings from four to seven minutes after injection; the second, ten to twenty minutes; the third, fifty to sixty minutes; the fourth, two to three hours; and the fifth, four to twelve hours.

## SUMMARY

1. A study has been made of the effect of nephrectomy on the response to renin in unanesthetized rats.

2. Nephrectomized rats have been found to be abnormally sensitive to the pressor effects of renin, both as to degree and duration.

3. The intact kidney, from which the pressor substance, renin, is extracted, appears to possess the property, in vivo, of counteracting, in some manner, the effect of this same substance when it is artificially injected.

4. The method of extracting renin from the kidneys has been modified in a manner which seems to eliminate the initial depressor effect.

5. Unanesthetized rats have proved to be useful subjects for the study of the pressor effects of renin.

REFERENCES

1. Tigerstedt, R., and Bergmann, P. G.: Niere und Kreislauf, Skandinav. Arch. f. Physiol. **8**: 223, 1898.
2. Merrill, A., Williams, J. R., Jr., and Harrison, T. R.: The Site of Action of the Renal Pressor Substance, Am. J. M. Sc. **196**: 18, 1938.
3. Shaw, H. B.: Autointoxication; Its Relation to Certain Disturbances of Blood Pressure, Lancet **1**: 1295, 1375, 1906.
4. Williams, J. R., Jr., Harrison, T. R., and Grollman, A.: A Simple Method for Determining the Blood Pressure of the Unanesthetized Rat, J. Clin. Investigation **18**: 373, 1939.
5. Grossman, E. B.: Preparation of Extracts of the Renal Pressor Substance, Proc. Soc. Exper. Biol. & Med. **39**: 40, 1938.

# THE USE OF "EXERCISE TESTS" IN CONNECTION WITH VENOUS PRESSURE MEASUREMENTS FOR THE DETECTION OF VENOUS OBSTRUCTION IN THE UPPER AND LOWER EXTREMITIES

## A Preliminary Report

James Ross Veal, M.D., and Hugh Hudson Hussey, M.D.
Washington, D. C.

MEASUREMENT of the pressure in the peripheral veins is generally recognized as a diagnostic procedure of substantial value in a variety of diseases. The finding of an elevated pressure in the antecubital veins is sometimes the only means of detecting with certainty the presence of congestive heart failure. In obvious cases, in which it would be superfluous as a diagnostic test, it may still be used to advantage in gauging the severity of the heart failure and in following its progress. Measurement of the venous pressure is similarly useful in cases of acute and chronic cardiac compression. Comparisons of the pressures in the veins of the four extremities are helpful in the localization and diagnosis of arteriovenous fistula and of diseases causing partial or complete occlusion of one of the venae cavae or its branches. Venous pressure measurements are useful in the diagnosis of mediastinal lesions (especially mediastinal tumor), pleural and pulmonary diseases which alter the intrapleural pressure, intra-abdominal tumors, cirrhosis of the liver, ascites, and localized obstruction of the peripheral veins. In view of the fact that local lesions of the peripheral veins are so common (especially such conditions as thrombosis, phlebitis, and a varicose state), it is somewhat surprising that the applicability of venous pressure measurements to the diagnosis and study of these lesions has received comparatively little mention in the literature.

The term "venous pressure" requires some definition in order that it may be perfectly understood. It is used most commonly in connection with measurements which are referred to the level of the right auricle as a zero point for hydrostatic pressure and are obtained with the patient in a standard supine position. It has been suggested[1] that when the position of the right auricle is taken into consideration, the venous pressure be designated as "general" venous pressure. The term "local" venous pressure is reserved for measurements which are made without reference to the position of the heart or the posture of the patient, and with the zero point at the level of the vein that is being studied. In this paper, the term "venous" pressure will be considered to mean "general" venous pressure, unless otherwise stated.

From the Surgical Service, Gallinger Municipal Hospital, and the Department of Medicine, Georgetown University School of Medicine, Washington, D. C.
Received for publication Jan. 12, 1940.

There are three principal methods for estimating the peripheral venous pressure. The first of these consists in direct inspection and palpation of the vein. The second measures the pressure necessary to produce collapse of the vein or to prevent its filling. This is the so-called indirect method. The third measures the pressure exerted through a needle inserted into the vein in terms of the height of a column of liquid sustained by this pressure. This is the so-called direct method. The first two of these three methods are inaccurate and inadequate in several ways which need not be enumerated here. The direct method, on the other hand, is not only reasonably accurate when carefully used, but is entirely adequate to meet practically all requirements for measurement of the venous pressure.

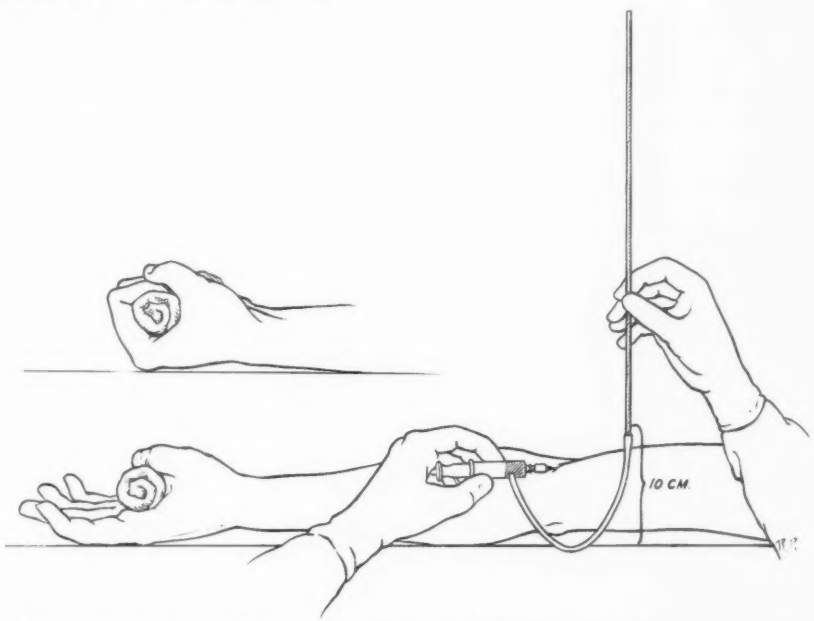



Fig. 1.—Apparatus and "exercise test" for studying antecubital venous pressure.

With certain exceptions, to be noted, the apparatus (Fig. 1) devised by Griffith, Chamberlain, and Kitchell[2] was used in these studies for measurement of the venous pressure in the antecubital or femoral vein. The apparatus consists of a 19-gauge needle and a 2 c.c. syringe with a sidearm to which a calibrated glass measuring tube of 4 mm. bore is connected by means of suitable rubber tubing. The other end of the glass tube is connected by means of another short piece of rubber tubing to a glass reservoir. The entire apparatus can be sterilized by boiling. Physiologic salt solution is placed in the reservoir and allowed to fill the entire apparatus, which is then ready to use. The patient is allowed to rest in the supine position for from fifteen to thirty minutes before measurement of his venous pressure is attempted. The arm in which the measurement is to be made is abducted to an angle of about 45°, and the needle is introduced into one of the veins of the antecubital fossa. The plunger of the syringe is drawn back, allowing saline to run through the sidearm into the syringe, and thence into the vein. Next, the reservoir is detached from the apparatus, and the zero point of the calibrated tube is placed

10 cm. above the skin of the patient's back. This reference point has been shown by Lyons, Kennedy, and Burwell[1] to be approximately level with the right auricle. The level of the column of saline falls, fluctuating somewhat with respiration, and stops at a point which indicates the height of the venous pressure in terms of millimeters of saline. Using this technique, it has been found that normal persons have a venous pressure of from 50 to 150 mm. This constitutes the basal venous pressure.

In some cases of mild or potential right ventricular failure, the venous pressure may be within normal limits. In such cases, special tests have been devised for verifying the existence of the heart failure. For example, raising the legs while the trunk remains horizontal has been shown to produce a rise of 30 mm., or more, in the venous pressure of patients with heart failure, but this maneuver has little or no influence on the venous pressure of normal persons.[3] Similar effects are obtained when the right upper quadrant of the abdomen is compressed for about a minute.[4] Also, it has been suggested[5] that the effect of exercise on venous pressure might be helpful in the detection of mild or incipient heart failure. All of these special tests record the venous pressure under practically basal conditions. As far as we have been able to discover, there has been no report of a diagnostic test which employs venous pressure measurements *during* exercise of the patient or a portion of his body.

The usefulness of venous pressure measurements in the differentiation of edema caused by lymphatic obstruction from that caused by venous obstruction was clearly shown by one of us in a study of cases of edema of the arm following radical mastectomy.[6] However, in some of these cases venograms revealed obstruction of the main venous channels and what seemed to be an inadequate collateral circulation, but the basal venous pressure in the edematous extremity was within normal limits. Moreover, there was an increase in the edema when the patient was allowed full use of the arm. In other cases in which there was no edema as long as the arm was kept at rest, edema would appear after vigorous exercise for a day. Therefore, it seemed obvious in these cases that the collateral circulation was adequate for the venous return while the arm was at rest, but not for the greatly increased return required by exercise. Similar observations were made in cases of traumatic thrombosis of the axillary and subclavian veins.

Judging from these studies, measurement of the basal venous pressure was misleading because it seemed to indicate that there was no venous obstruction, although the latter was actually demonstrated by means of the venogram, the obvious enlargement of collateral veins, and the presence of edema. Furthermore, it is important to recognize that, in these cases, exercise of the affected arm was the factor which demonstrated the inadequacy of the collateral circulation and determined the degree of venous obstruction. As we have already said, provision for the venous return may be adequate with the arm at rest,

but seriously inadequate during exercise. Therefore, a method which would reveal the changes in venous pressure during exercise of the affected arm would indicate more accurately the presence and degree of venous obstruction. Measurement of the venous pressure during exercise would be more valuable than a measurement obtained in the usual way immediately after exercise, because in some cases of peripheral venous obstruction the effects of exercise on the venous pressure might be quite transitory. With these facts in view, we have devised the simple procedures which are to be described in this paper.

### THE "EXERCISE TEST" IN THE UPPER EXTREMITY

*Method.*—The pressure in the antecubital vein is measured by the method described above. With the venous pressure apparatus still in use, a roll of bandage is placed in the patient's hand on the same side on which the measurement is being taken. The patient is told to close and open his hand, squeezing the bandage tightly with each contraction and relaxing completely when the hand is open (Fig. 1). This is continued for one minute, during which the patient usually will have clenched his fist from thirty to forty times. It is important to instruct the patient to restrict his exertion to the arm, and to try to continue breathing regularly and evenly.

We have found in some cases of obstruction of the axillary and subclavian veins that the venous pressure may rise so high during the exercise test that it cannot be recorded conveniently with the saline manometer. In such cases it is possible to substitute a mercury manometer by means of a three-way stopcock (Fig. 2). In making readings during the exercise test, if it is found that the venous pressure is rising too high for measurement by the saline manometer, the lever of the stopcock is turned so that the pressure is measured in millimeters of mercury while the exercise continues. Later this measurement can be translated easily into millimeters of saline.

*Clinical Application.*—When this exercise test is applied to normal persons, the venous pressure usually rises a few millimeters above the basal level. We have not observed a rise of more than 10 mm. of saline in any normal subject, and, at the conclusion of the exercise, the pressure returns very promptly to, or slightly below, the basal level. In some cases no rise can be demonstrated, and the pressure may even fall slightly during the exercise. Prolongation of the exercise does not materially influence the results.

In cases of congestive heart failure the venous pressure may be initially high, but the effect of the exercise test is the same as in normal subjects. Apparently, the type of venous obstruction that occurs in heart failure has no influence on the exercise test. This observation seems to us to be of some importance. As will be seen, it may be an additional means of differential diagnosis in cases of edema in which the venous pressure is elevated.

The effects of the exercise test are quite different in cases of local obstruction of the axillary or subclavian vein. In most of the cases which we have had the opportunity to observe, venographic studies have been employed to confirm the presence and location of the obstruction. Whether or not the venous pressure is initially high in the affected arm.

it rises steadily during the exercise test. The pressure may reach a peak within the usual one-minute period of exercise, or may not attain its maximum level unless the exercise is continued for several minutes, or even longer. During the test, when the patient's hand is relaxed, the pressure sometimes continues to rise, or it may remain unchanged until the next manual contraction. The rise of venous pressure in every case of this type that we have studied has exceeded 50 mm. of saline; in one case the rise was 962 mm.

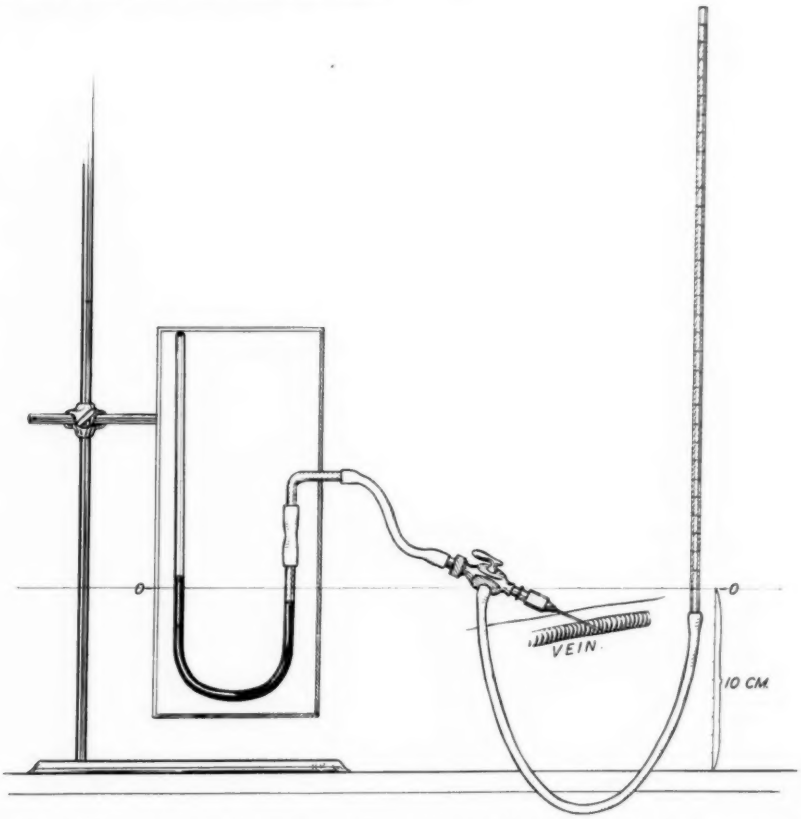



Fig. 2.—Apparatus for substituting a mercury for a saline manometer during measurement of venous pressure.

Whereas, in normal subjects, completion of the exercise test is followed by a prompt return of the venous pressure to, or below, its initial level, in the cases of venous obstruction the fall is slower, and the pressure may not reach the initial level for several minutes. The rapidity of the fall apparently depends upon the degree of venous occlusion and the extent of the collateral circulation. When the obstruction is severe and collateral vessels are few, the venous pressure may remain above the initial level for several minutes. When there are numerous collateral vessels, the fall is more rapid, but the return to the original level is never so prompt as in normal persons.

The sensitivity of the exercise test and its value in diagnosis are demonstrated in the reports of the following cases.

## REPORT OF CASES

CASE 1.—The patient was a 65-year-old white woman who was receiving treatment for congestive heart failure secondary to coronary arteriosclerosis. She developed tenderness and prominence of the veins of the left upper extremity and slight edema of the left hand. These changes were believed to be caused by localized thrombophlebitis of the axillary vein. The pressure in the antecubital veins was 265 mm. of saline on the left, and 235 mm. on the right. During performance of the exercise test for one minute, the pressure rose to 360 mm. on the left and 250 mm. on the right. On cessation of exercise, the pressure returned to its original levels within about thirty seconds. These results were interpreted as confirmatory of the diagnosis of heart failure, with localized venous obstruction. One week after these original measurements were made, the patient had improved considerably. The tenderness of the veins of the left arm and the edema of the hand had disappeared. At this time the pressure was initially the same in the antecubital veins of the two arms. However, the exercise test produced a response almost identical with that obtained on the first occasion. The fact that the venous pressure was initially the same in the two arms indicated that there had been some lessening of the localized venous obstruction, but the exercise test showed that the obstruction had not disappeared entirely.

CASE 2.—This patient was a 65-year-old negress who had had a radical mastectomy, followed by deep roentgen therapy, for carcinoma of the left breast. Edema of the left upper extremity appeared several weeks after the operation, and it had persisted during the ensuing three years. The edema was aggravated by activity, especially by work requiring much use of the arm, and was relieved to a large extent by rest. Examination three years after the mastectomy was performed showed that the left upper extremity was about twice the thickness of the right, and that this enlargement was caused by edema. There was a large, deeply contracted scar in the left axillary region. The causal relationship of this scar to the edema seemed obvious. The basal venous pressure was 130 mm. of saline in the left, and 100 mm. of saline in the right, antecubital vein. During the exercise test the pressure on the left side rose so high that it was necessary to utilize the mercury manometer in order to measure it. When the necessary calculation had been made, it was found that the pressure had risen to 962 mm. of saline after exercise for one minute. The return of the pressure to its initial level was delayed; one minute after stopping the exercise it was still 182 mm. of saline (Fig. 3). The exercise test had practically no effect upon the venous pressure in the right arm.

In this case, basal venous pressure measurements were of little value in the endeavor to prove that the edema of the left arm was caused by venous obstruction. However, the exercise test clearly substantiated this impression, which was further verified by venography.

CASE 3.—The patient, a 46-year-old negro, was admitted to Gallinger Municipal Hospital July 13, 1939. He complained only of swelling of the face, which had been present for ten days; his history was otherwise irrelevant except for the vague possibility that he might have had syphilis. The only important abnormalities were edema of the face and left upper extremity, dilatation of the veins of the arms and upper part of the thorax, and a strongly positive blood Kahn reaction. The suspicion that he might have a mediastinal tumor was not confirmed by roentgenologic examination, which showed only dilatation of the superior vena cava. The pressure in the antecubital veins was 510 mm. of saline on the left, and 500 mm. on the right. Compression of the right upper quadrant of the abdomen caused a fall on both sides. The femoral venous pressure was 70 mm. of saline. During the exercise test the venous

pressure rose to 590 mm. in both arms. After exercise was stopped, the pressure returned very slowly to its original level; it was still somewhat elevated at the end of three minutes. These observations were thought to prove beyond doubt that the superior vena cava was obstructed, but that the flow of blood from the inferior vena cava was unimpeded. Intensive antisyphilitic treatment with neoarsphenamine and potassium iodide was started on July 22, and by the middle of August all of the edema had disappeared. On August 8, the venous pressure in the right arm was 340 mm. During the exercise test it rose to 500 mm., and, when the exercise was continued for three minutes, it reached 615 mm. On August 31, the pressure in the antecubital veins was 320 mm. on the left, and 330 mm. on the right. The pressure rose to 520 mm. during the exercise test, but returned to its initial level within two minutes after exercise was stopped (Fig. 4). The patient was discharged from the hospital soon after the last measurements were made.

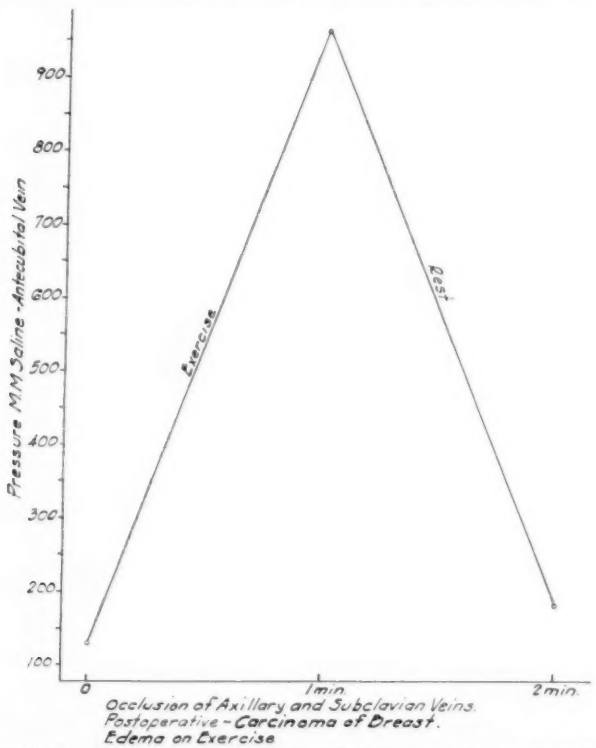



Fig. 3.—Antecubital venous pressure during exercise in a case of obstruction of the axillary and subclavian veins (Case 2).

In this case, obstruction of the superior vena cava was apparently ameliorated to some extent by antisyphilitic treatment. The venous pressure measurements, including those made during the exercise test, were a means of confirming the diagnosis and of demonstrating objectively that the patient's improvement was the result of lessening of the venous obstruction.

CASE 4.—This patient was a 39-year-old white man who had been examined at the Georgetown University Hospital in October, 1939, at which time a diagnosis of constrictive pericarditis, with calcification of the pericardium, was made. Subsequently, he was sent to Dr. Claude S. Beck, at Cleveland, for operative treatment of the cardiac compression. The initial venous pressure was 290 mm. of saline in the right antecubital vein, and 295 mm. in the left. During the exercise

test the pressure rose to 340 mm. on the right side, and 345 mm. on the left. The time required for the pressure to return to its initial levels was 3¾ minutes in both arms.

This case demonstrated that chronic cardiac compression alters antecubital venous pressure in the same way as localized venous obstruction. The exercise test in such cases should serve as an additional means of differentiation from congestive heart failure.

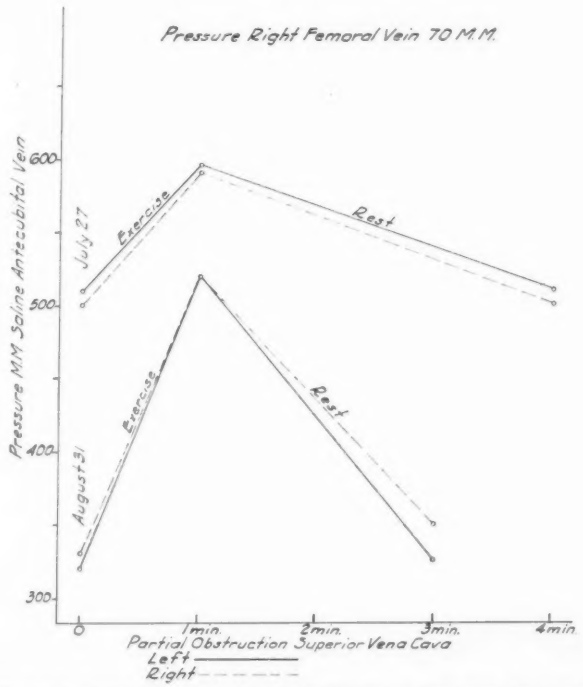



Fig. 4.—Effect of exercise on the antecubital venous pressure in a case of partial occlusion of the superior vena cava. Note the rapid rise in the pressure during exercise, and the gradual fall during the rest period (Case 3).

## THE "EXERCISE TEST" IN THE LOWER EXTREMITY

There have been comparatively few clinical measurements of venous pressure in the lower extremities. The reason is that such measurements are most commonly made in cases of heart failure, and in this condition the antecubital vein is the most satisfactory one to use. Estimation of the pressure in the femoral or saphenous vein is recommended in the study of arteriovenous fistula of the lower extremity,[7] and to help detect obstruction of one of the venae cavae without obstruction of the other.[8] In the latter case, it is necessary to compare the pressure in the antecubital vein with that in the femoral.

Measurement of the femoral venous pressure is made with the same apparatus and technique which are used for the upper extremity, except that a tourniquet is not needed. The needle can easily be introduced through the skin into the femoral vein at a point about 1 inch

distal to the inguinal ligament, just medial to the femoral artery. The angle at which the needle is introduced will vary, depending on whether the vein is superficial or deep. This method has found practically no application in the study and diagnosis of localized venous obstruction in the lower extremity.

The symptoms and signs of obstruction of the iliac and femoral veins are often clear-cut and easily recognized. However, it may be difficult to be sure whether or not there is slight obstruction, especially when clinical evidence of phlebitis or venous collateral circulation is lacking. Similarly, in cases of unilateral or bilateral edema of the lower extremities, it may be difficult to discover the pathogenesis of the edema. Measurement of the pressure in the femoral vein, or in one of the superficial veins of the leg, with the patient supine, may be of no assistance in such cases, and the results may even be misleading. Just as in the upper extremity, the venous pressure under relatively basal conditions may not be altered by partial obstruction of the veins. This is especially true in conditions in which the obstruction does not become entirely effective until the patient assumes the upright position, as, for example, when there is compression of the pelvic veins by a tumor. Moreover, measuring the venous pressure in the leg or thigh while the patient is standing is usually not helpful in the diagnosis of venous obstruction because such pressures vary widely in normal persons, and because only the "local" venous pressure can be measured in this way. There is no way to express such a measurement in terms which take into consideration the position of the right auricle as a reference point. However, a record of the changes which take place in the "local" venous pressure of the lower extremity during exercise in the upright position is useful in the detection of venous obstruction. This kind of record can be obtained by using the popliteal vein.

The popliteal vein is formed by the junction of the anterior and posterior tibial veins at the lower border of the popliteus muscle. It receives the lesser saphenous vein and a few minor tributaries. It is about the size of the axillary vein, and is, of course, fully distended when one stands on one's feet. It can be easily punctured for venous pressure studies if careful attention is paid to certain anatomic landmarks. The vein lies superficial to the popliteal artery and medial to the tibial nerve. The upper third of the vein is covered by the semimembranosus and semitendinosus muscles, and the lower third by the gastrocnemius muscle. It is most superficial in the middle third, where it is covered only by the deep fascia, subcutaneous tissue, and skin. This part of the vein is most accessible for venipuncture, and particularly for performance of the exercise test, because, when a needle is inserted into the vein at this point, it will not be affected by contraction of the muscles (Fig. 5).

*Method.*—The apparatus for measurement of the popliteal venous pressure consists of a mercury U-tube manometer, one arm of which is straight, and the other

arm bent at an angle to facilitate attachment of a piece of rubber tubing. A millimeter scale is affixed beside the straight arm for the purpose of recording pressure. Readings from this scale must be doubled, of course, in order to obtain the actual pressure in millimeters of mercury. The other arm is filled completely, from the surface of the column of mercury to its tip, with 2.5 per cent sodium citrate solution. The height of the column of mercury beside the millimeter scale is noted. Next, a sterile length of rubber catheter, with a needle adaptor in one end, is filled completely, by means of a sterile 5 c.c. syringe, with sterile 2.5 per cent sodium citrate solution. This tubing is clamped with a small hemostat, and its free end is then slipped on the designated arm of the manometer, care being taken to exclude air bubbles from the system. The manometer is adjusted on its supporting stand in such a way that the zero level of the column of mercury is on a plane with the point at which the venipuncture is to be made. This adjustment is accomplished by means of a carpenter's level.

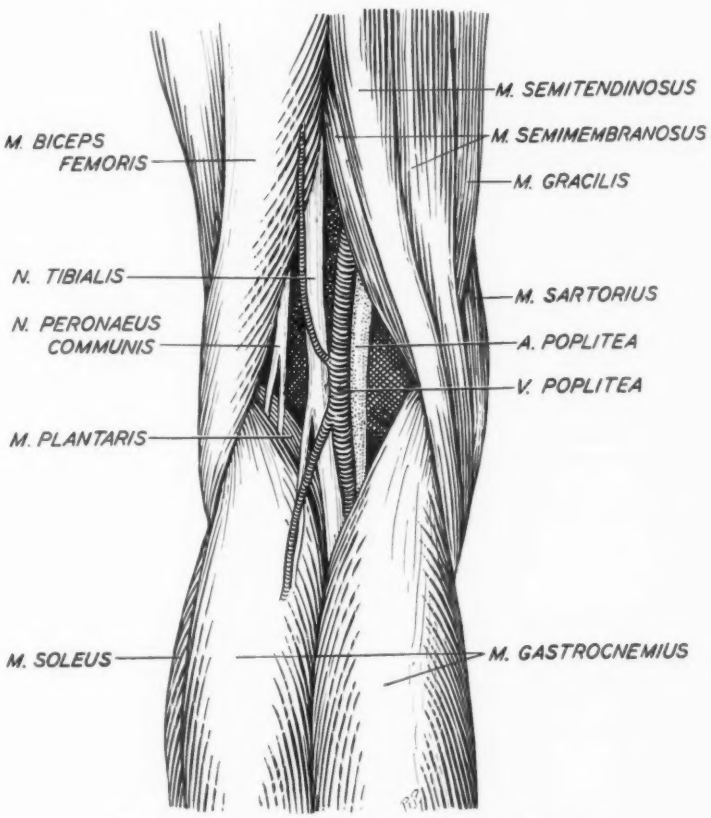



Fig. 5.—Anatomic relations of the popliteal vein.

The patient is instructed in the procedure of the test and is shown how to perform the exercise. He stands erect, with feet slightly apart, on a smooth table set against the wall, where supports are provided for his hands. The lower halves of the thighs, and the legs, are exposed; the shoes and stockings are removed. Standing behind the patient, the operator palpates the lower border of the patella with his index finger, and locates with the thumb of the same hand a point on the same level, just medial to the lateral head of the gastrocnemius and the plantaris muscles. After appropriate sterilization of the skin, a wheal is produced at this point with

1 per cent solution of novocain. A 19-gauge, 1½-inch needle, attached to a 5 c.c. syringe, is inserted through the anesthetized area and pushed straight forward until the popliteal vein is punctured. During the insertion of the needle, traction is exerted upon the plunger of the syringe, so that entrance of the needle into the vein can be recognized instantly by the spurt of dark-red blood into the syringe. The depth to which the needle must be inserted varies somewhat in different subjects, but is usually about 1 inch. The patient is warned that he may experience a sharp pain radiating down his leg. He is cautioned not to move his leg, but to inform the operator of the discomfort. This happens not infrequently; it is caused by pricking the tibial nerve, which lies close to the lateral surface of the vein. The pain is only momentary, and is an indication that the needle should be reinserted slightly more medially. When the popliteal vein has been entered, the syringe is detached from the needle, and the adaptor of the venous pressure apparatus is connected to the needle. Loss of a small amount of blood is unavoidable during this transfer. Finally, the clamp is removed from the tubing of the apparatus.

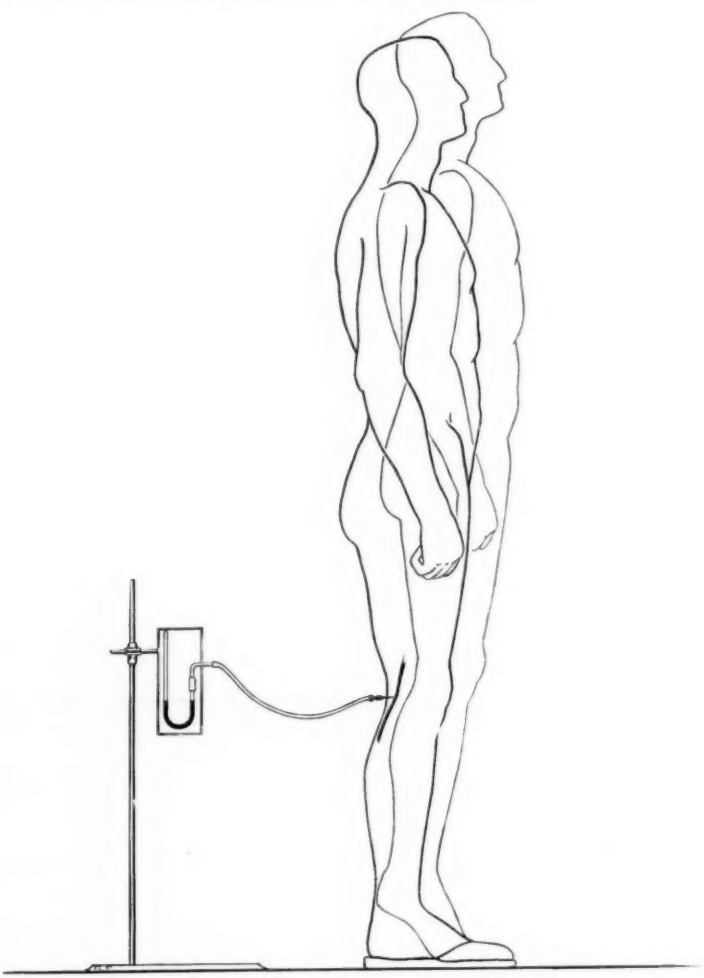


Fig. 6.—Apparatus and technique for "exercise test" in measuring popliteal venous pressure.

The column of mercury in the manometer will quickly come to a level which indicates the local pressure in the vein. The height of this level is recorded as the initial venous pressure. The patient then begins the exercise, which consists in rising on his toes repeatedly (twenty to thirty times) for one minute (Fig. 6). It is important that he use the hand supports on the wall only for the purpose of steadying himself, and not as a means of assisting in the exertion, that he breathe regularly during the exercise, and that he relax the muscles of his legs each time his heels are lowered to the surface of the table. During the test it is necessary for the operator to support the rubber tubing of the apparatus with his hand, in order to keep the needle horizontal and prevent it from slipping. The changes in venous pressure during exercise are recorded, and the pressure is observed for a short time after exercise has ceased. The needle is then withdrawn, and firm pressure is applied for about a minute at the site of venipuncture. The patient is required to walk around the room for a few minutes at the conclusion of the test in order to minimize the likelihood of venous thrombosis.

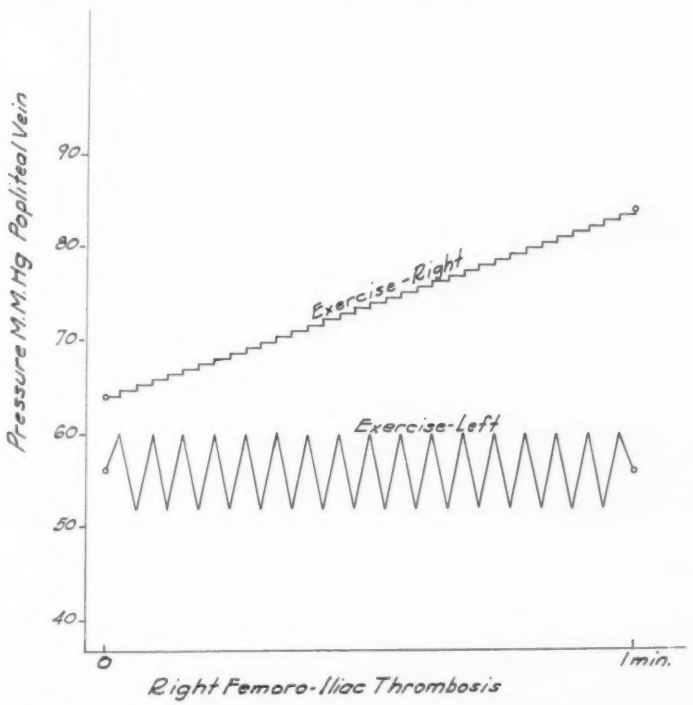



Fig. 7.—Steady rise in popliteal venous pressure during exercise in a case of obstruction of the right iliac and femoral veins. Note the fluctuations in the popliteal pressure in the normal lower extremity (Case 5).

*Clinical Application.*—In the absence of obstruction of the veins of the lower extremity, the exercise test has little effect upon the local pressure in the popliteal vein. Usually, the column of mercury will fluctuate slightly, rising each time the patient moves up on his toes, and falling when he lowers himself. The average range of this fluctuation is about 4 mm. above and below the initial pressure. In some cases the exercise produces only a slight fall in the venous pressure.

We are at present engaged in studying more thoroughly the influence of venous obstruction upon the results of the exercise test, but a preliminary idea of its clinical application in cases of this type can be gained from the following case report.

CASE 5.—The patient, a 36-year-old negro, had thromboangiitis obliterans and thrombophlebitis of the vessels of the right leg and thigh. There was moderate edema of the affected extremity. The left lower extremity was apparently normal. In the left popliteal vein the initial pressure was 56 mm. of mercury. During exercise the pressure fluctuated between 52 and 60 mm. It returned promptly to the initial level when the exercise was stopped. In the right popliteal vein the initial pressure was 64 mm. During exercise the pressure rose gradually (Fig. 7) to 84 mm. When exercise ceased the pressure returned promptly, for a moment, to 64 mm., but then rose again slowly to 76 mm., where it remained, showing no tendency to fall during the ensuing several minutes of observation.

## DISCUSSION

The "exercise tests" which have been described are practical, simple, and easy to apply. The advantage of their use in connection with measurement of the venous pressure is obvious in cases of local venous obstruction, in which the venous pressure is normal during rest and high only during exertion. In such cases, measurement of the venous pressure by the usual methods may give results which are actually misleading. The tests are apparently sensitive enough to detect venous obstruction when other signs are lacking. They are useful in distinguishing between various types of peripheral edema. In this connection, their value is further enhanced by the fact that heart failure has no effect upon the "exercise test" on the upper extremity. Moreover, the positive response to the test in cases of chronic cardiac compression and compression of the superior vena cava by mediastinal tumors, or other lesions, renders it useful in the differentiation of these conditions from heart failure, in doubtful cases.

## SUMMARY

1. The fact that it is impossible, in some cases, to detect the presence of localized venous obstruction by measuring the basal venous pressure is discussed.

2. A description is given of simple methods which enable one to measure "general" or "local" venous pressure in the antecubital vein, and "local" venous pressure in the popliteal vein, during exercise.

3. The effects of these "exercise tests" upon the venous pressures of normal persons, patients with heart failure, and patients with localized venous obstruction are presented.

4. The value of the "exercise tests" in the endeavor to demonstrate the presence of localized venous obstruction in the upper and lower extremities is illustrated by means of case reports.

## REFERENCES

1. Lyons, R. H., Kennedy, J. A., and Burwell, C. S.: The Measurement of Venous Pressure by the Direct Method, AM. HEART J. **16:** 675, 1938.
2. Griffith, G. C., Chamberlain, C. T., and Kitchell, J. R.: Simplified Apparatus for Direct Venous Pressure Determination Modified from Moritz and von Tabora, Am. J. M. Sc. **187:** 371, 1934.
3. Levin, E.: Provoked Venous Hypertension as Sign of Cardiac Insufficiency; Influence of Azoulay Position, Semana méd. **2:** 915, 1934.
4. Oppenheimer, B. S., and Hitzig, W. M.: The Use of Circulatory Measurements in Evaluating Pulmonary and Cardiac Factors in Chronic Lung Disorders, AM. HEART J. **12:** 257, 1936.
5. Pla, J. C.: Classification of Venous Hypertension, Rev. sud.-am. de méd. et de chir. **1:** 283, 1930.
6. Veal, J. R.: The Pathologic Basis for Swelling of the Arm Following Radical Amputation of the Breast, Surg., Gynec. & Obst. **67:** 752, 1938.
7. Villaret, M., Saint-Girons, F., and Justin-Besancon, L.: Peripheral Venous Pressure, Paris, 1930, Masson.
8. Hussey, H. H.: The Effect of Mediastinal Lesions on Pressures in the Antecubital and Femoral Veins, AM. HEART J. **17:** 57, 1939.

# GALVANOMETRIC POTENTIALS OF THE EXTREMITIES AND OF THE THORAX IN CONGENITAL DEXTROCARDIA

CHARLES E. KOSSMANN, M.D.
NEW YORK, N. Y.

IN PRECORDIAL electrocardiograms of normal subjects it has been shown that the deflection analogous to the intrinsic deflection of direct leads[1] occurs, on the average, 0.16 sec. later in leads from the left side of the precordium than in leads from the right side.[2, 3] This has been interpreted to mean that excitation reaches the epicardial surface of the anterior wall of the right ventricle earlier, on the whole, than it reaches the corresponding surface of the left ventricle. It has been concluded, largely from experimental observations,[4] that the difference is due principally to the greater thickness of the left ventricle in normal adults. Further support for the truth of this assumption can be obtained in several ways. One of the simplest is to measure the time of the intrinsicoid deflection[1] in the precordial electrocardiograms of subjects who are normal in all respects except that the position of their cardiac chambers is reversed. The desired conditions are found in cases of uncomplicated, congenital dextrocardia.

## METHODS

Nine subjects were studied, but four were excluded because the dextrocardia was complicated by rheumatic, hypertensive, or arteriosclerotic heart disease. Of the remaining five, all of whom had complete situs inversus viscerum, four were women whose ages ranged from 20 to 32 years, and the other was a boy, aged 12 years. One of the women (Case 4) was in the fifth month of a uterine pregnancy. None of the subjects displayed any clinical, radiologic, or electrocardiographic evidence of cardiac disease, other than dextrocardia.

Two string galvanometers, arranged to record simultaneously on the same film, were employed.[5] The first was connected to the balanced plate circuit of a single-stage vacuum-tube amplifier. It was used to record the following (upper curve in each illustration): standard Leads I, II, and III; the potential variations of the right arm ($V_R$), of the left arm ($V_L$), and the left leg ($V_F$); the potential variations of nine points on the thorax, namely, $V_1$, fifth rib at the right sternal edge; $V_2$, fifth rib at the left sternal edge; $V_3$, fifth intercostal space in the left parasternal line; $V_4$, fifth intercostal space in the left midclavicular line; $V_5$, sixth rib in the left anterior axillary line; $V_E$, tip of the ensiform process; $V_6$,* fifth intercostal space in the right parasternal line; $V_7$, fifth intercostal space in the right midclavicular line; $V_8$, sixth rib in the right anterior axillary line. The string sensitivity when the standard leads and the extremity potentials were recorded was normal (1 cm. = 1 mv.); when the thoracic potentials were recorded it was half normal (1 cm. = 2 mv.). The extremity and thoracic potentials were obtained by the method of Wilson, Johnston, Macleod, and Barker.[6] In Case 1 the connections to the galvanometer were so made that positivity of the exploring

From the Department of Medicine, New York University College of Medicine, and the Third (New York University) Medical Division of Bellevue Hospital, New York.
Received for publication Dec. 17, 1939.

*It is to be noted that Lead $V_6$ in this instance is not the lead of this designation described in the Standardization of Precordial Leads.[7]

electrode resulted in a downward movement of the string shadow. They were labeled, therefore, as if they were upside down (Figs. 1 and 2), in accordance

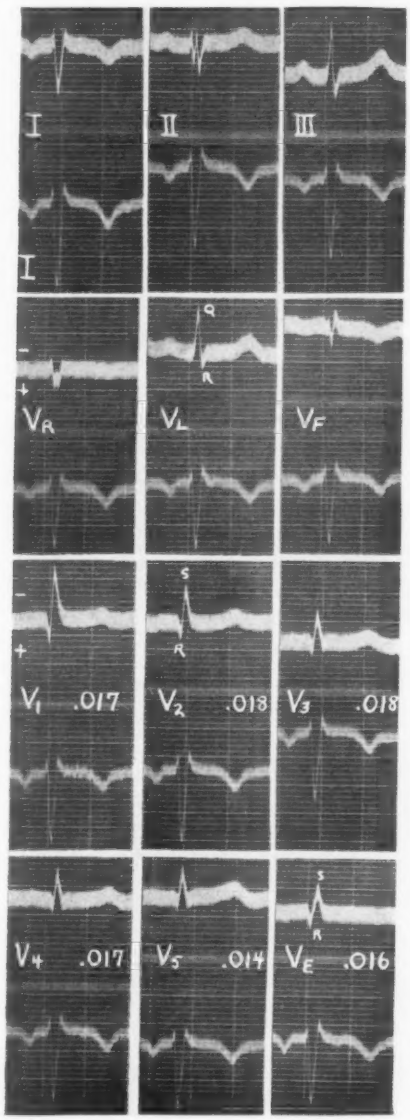



Fig. 1.—Standard electrocardiograms, extremity potentials, and potentials of the left border of the precordium and left side of the chest, in Case 1. The upper curve in each illustration shows, I, standard Lead I; II, standard Lead II; III, standard Lead III; $V_R$, $V_L$, and $V_F$ are the potential variations of the right arm, the left arm, and the left leg, respectively. These six curves were taken with the string at normal sensitivity (1 cm. = 1 mv.). The next six curves, which were taken with the string at half normal sensitivity (1 cm. = 2 mv.), represent the potential variations of the following thoracic points: $V_1$, fifth rib, right sternal edge; $V_2$, fifth rib, left sternal edge; $V_3$, fifth intercostal space, halfway between the left sternal edge and the left midclavicular line; $V_4$, fifth intercostal space in the left midclavicular line; $V_5$, sixth rib in the left anterior axillary line; $V_6$, tip of the ensiform process. The lower curve in each illustration is standard Lead I, taken with the string at normal sensitivity. The figure on each record is the time in seconds between the beginning of QRS in standard Lead I and the intrinsicoid (RS) deflection of the chest lead. The time intervals are 0.2 second.

with the recommendations of the Committee on Precordial Leads of the American Heart Association.[7] In the remaining four cases the potentials were recorded as recommended by the Committee.

The second galvanometer was used, in the usual way, to record standard Lead I at normal string sensitivity (lower curve in illustrations). The thoracic electrode was of German silver; it was circular, and measured 1.5 cm. in diameter. The electrodes on the extremities were rectangular plates of German silver, 5 cm. by 3.5 cm. Contact between the electrodes and the body was made with electrode jelly.*

In two cases (Nos. 1 and 3), small lead markers were placed on the points from which chest leads had previously been made, and teleroentgenograms were taken. In one case, large breasts prevented accurate recording of any but the three mid-thoracic leads (Fig. 3); in the other, a young boy, the relationship of the markers to the cardiac silhouette was similar to that shown in Fig. 3.

The time between the beginning of the intrinsicoid (RS) deflection of the thoracic leads and the beginning of QRS in Lead I was measured with a comparator designed by Capt. Elliott.*

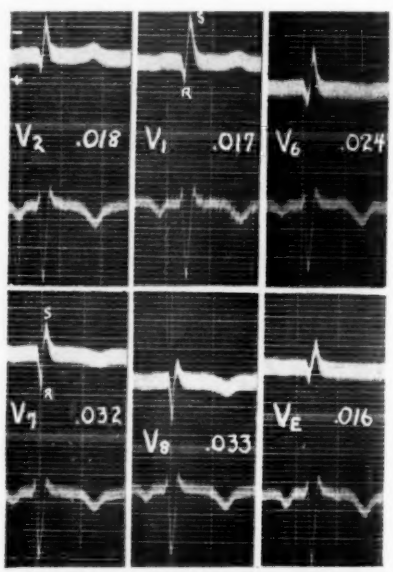



Fig. 2.—The potential variations of the precordium in Case 1. $V_1$, $V_2$, and $V_E$ are identical with similarly designated curves in Fig. 1. The other three curves show the potential variations of the following points: $V_6$, fifth intercostal space, halfway between the right sternal edge and the right midclavicular line; $V_7$, fifth intercostal space in the right midclavicular line; $V_8$, sixth rib in the right anterior axillary line. The curves have been arranged in the order shown for the purpose of emphasizing their mirror-image similarity to those obtained from the left side of the chest of a normal subject. Time intervals and lower records as in Fig. 1.

## OBSERVATIONS

The standard electrocardiograms were normal in all respects, except for complete inversion of Lead I. The minimum, maximum, and mean voltages of the ventricular deflections in the standard and special electrocardiograms are given in Table I.

The potential variations of the left arm ($V_L$) were principally negative (Fig. 1). A positive deflection (R wave), if present, was small.

*Cambridge Instrument Co.

TABLE I

SIZE OF THE VENTRICULAR DEFLECTIONS IN THE STANDARD AND SPECIAL LEADS IN 5 CASES OF DEXTROCARDIA (MEASUREMENTS IN TENTHS OF A MILLIVOLT)

| LEAD | Q | | | R | | | S | | | T | | | RS* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | MIN. | MAX. | MEAN | MIN. | MAX. | MEAN | MIN. | MAX. | MEAN | MIN. | MAX. | MEAN | MIN. | MAX. | MEAN |
| I | 0 | 3.0 | 0.60 | 1.0 | 1.5 | 1.30 | 0 | 12.0 | 8.10 | −3.0 | −2.0 | −2.40 | 4.5 | 13.5 | 10.40 |
| II | 0 | 1.0 | 0.20 | 1.5 | 7.0 | 3.20 | 0 | 7.0 | 3.60 | 0 | 2.0 | 0.90 | 4.0 | 8.5 | 7.00 |
| III | 0 | 0.5 | 0.20 | 3.0 | 10.0 | 7.80 | 0 | 2.5 | 1.10 | 2.0 | 5.0 | 2.90 | 4.0 | 12.5 | 9.00 |
| $V_R$ | 0 | 1.0 | 0.36 | 1.0 | 5.0 | 2.90 | 0 | 4.0 | 1.00 | 0 | 1.0 | 0.70 | 2.0 | 6.0 | 3.90 |
| $V_L$ | 0 | 7.0 | 2.60 | 0 | 1.0 | 0.60 | 0 | 5.5 | 2.10 | −2.5 | −1.0 | −1.60 | 3.5 | 8.0 | 5.30 |
| $V_F$ | 0 | 0.5 | 0.10 | 0.5 | 5.0 | 2.10 | 0 | 3.0 | 1.20 | 0.5 | 2.0 | 1.10 | 1.5 | 4.0 | 3.40 |
| $V_1$ | 0 | 0 | 0 | 5.0 | 13.0 | 8.20 | 11.0 | 36.0 | 21.40 | −1.0 | 2.0 | 0.30 | 18.0 | 49.0 | 27.60 |
| $V_2$ | 0 | 0 | 0 | 2.5 | 7.0 | 4.50 | 6.0 | 24.0 | 13.40 | −2.0 | −0.5 | −1.40 | 8.5 | 37.0 | 21.30 |
| $V_3$ | 0 | 0 | 0 | 1.0 | 5.0 | 2.72 | 4.0 | 15.0 | 9.0 | −3.0 | −0.5 | −1.70 | 5.0 | 20.0 | 11.72 |
| $V_4$ | 0 | 0 | 0 | 0.5 | 3.5 | 2.00 | 2.0 | 8.5 | 6.70 | −3.0 | 0 | −1.60 | 2.5 | 12.0 | 8.70 |
| $V_5$ | 0 | 0 | 0 | 0.5 | 2.0 | 1.20 | 0 | 8.0 | 4.80 | −3.0 | 0 | −1.20 | 0.5 | 9.5 | 6.00 |
| $V_E$ | 0 | 1.0 | 0.20 | 3.0 | 6.0 | 4.10 | 2.0 | 16.0 | 9.40 | 0 | 0.5 | 0.20 | 5.0 | 22.0 | 13.50 |
| $V_6$ | 0 | 0 | 0 | 6.0 | 13.0 | 9.0 | 5.0 | 18.0 | 11.80 | 0.5 | 4.0 | 2.70 | 11.0 | 31.0 | 20.80 |
| $V_7$ | 0 | 1.0 | 0.30 | 8.0 | 38.0 | 17.20 | 4.0 | 8.0 | 6.30 | 2.0 | 6.0 | 4.40 | 16.0 | 43.5 | 23.50 |
| $V_8$ | 0 | 2.0 | 0.80 | 8.0 | 22.0 | 14.60 | 0 | 5.5 | 2.50 | 2.0 | 7.0 | 4.40 | 11.0 | 22.0 | 17.10 |

*Or QR, depending on which is larger

The T wave was negative. The left arm was, as might be expected, electrically similar to the right arm in a normal subject.

The mean potential of the right arm during the inscription of QRS was negative, zero, or positive, depending upon whether the mean electrical axis* was deviated slightly, moderately, or markedly to the right. A reverse relationship was found between the mean potential of the left leg and the electrical axis (Table II).

TABLE II

THE ANGLE ALPHA IN FIVE CASES OF DEXTROCARDIA, ARRANGED TO SHOW THE EFFECT OF ITS INCREASE ON THE MEAN POTENTIAL OF THE RIGHT ARM ($V_R$) AND OF THE LEFT LEG ($V_F$) WHEN THE MANIFEST POTENTIAL, E, IS RELATIVELY CONSTANT. VALUES FOR E, $V_R$, AND $V_F$ ARE GIVEN IN TENTHS OF A MILLIVOLT

| CASE | ANGLE ALPHA | $E = \frac{e_1}{\cos \alpha}$ | LEAD $V_R$ | LEAD $V_F$ |
|---|---|---|---|---|
| 5 | +101° | 10.3 | −1 | 5 |
| 3 | +143° | 9.9 | 0 | 2 |
| 1 | +156° | 9.9 | 3 | 0 |
| 2 | +183° | 11.0 | 5 | −1 |
| 4 | +193° | 7.2 | 4 | 0 |

TABLE III

TIME OF ONSET OF INTRINSICOID (RS) DEFLECTION IN CHEST LEADS, WITH REFERENCE TO THE EARLIEST VENTRICULAR DEFLECTION OF LEAD I IN FIVE CASES OF DEXTROCARDIA. AVERAGES OF THESE FIGURES IN NORMAL SUBJECTS ARE INCLUDED AT FOOT OF TABLE FOR COMPARISON

| CASE | LEADS FROM RIGHT SIDE OF ANTERIOR THORAX | | | LEADS FROM MIDTHORAX ANTERIOR | | | LEADS FROM LEFT SIDE OF ANTERIOR THORAX | | |
|---|---|---|---|---|---|---|---|---|---|
| | $V_8$ | $V_7$ | $V_6$ | $V_1$ | $V_E$ | $V_2$ | $V_3$ | $V_4$ | $V_5$ |
| 1 | 0.033 | 0.032 | 0.024 | 0.017 | 0.016 | 0.018 | 0.018 | 0.017 | 0.014 |
| 2 | 0.040 | 0.040 | 0.037 | 0.019 | 0.014 | 0.015 | 0.014 | 0.016 | 0.016 |
| 3 | 0.037 | 0.034 | 0.024 | 0.022 | 0.019 | 0.023 | 0.025 | 0.021 | 0.020 |
| 4 | 0.034 | 0.034 | 0.022 | 0.023 | 0.019 | 0.021 | 0.016 | 0.018 | 0.018 |
| 5 | 0.028 | 0.032 | 0.016 | 0.014 | 0.015 | 0.008 | 0.009 | 0.008 | – |
| Means | 0.0344 | 0.0344 | 0.0246 | 0.0190 | 0.0166 | 0.0170 | 0.0164 | 0.0160 | 0.0170 |
| Means in normal subjects | 0.0167* | 0.0166* | 0.0184* | 0.0172 | 0.0249 | 0.0193 | 0.0314 | 0.0349 | 0.0326 |

*Means of 5 normal subjects. Remaining figures on this line represent the averages of 30 normal subjects.[3]

As the thorax was explored, all of the ventricular deflections changed in size, as shown in Table I. On the average, the R wave became taller as the exploring electrode was moved from the right side to the left side of the chest, and reached its maximum size in the lead from the right midclavicular line ($V_7$). The S wave was largest in the lead from the right sternal edge ($V_2$). It diminished in size as the distance between the right sternal edge and a lead on either side of it was increased. The same was true of the RS deflection, with the exception of Lead $V_7$, in which RS was slightly greater than in Lead $V_6$. In the

*The mean electrical axis was obtained by applying the method of Carter, Richter, and Greene[8] to the algebraic sum of QRS deflections in Leads I and III. "Mean electrical axis" was originally, and more accurately, determined from the area of the ventricular deflections.[9]

five cases, a Q wave was encountered once in Lead $V_E$, twice in Lead $V_7$, and three times in Lead $V_8$. The T wave was isoelectric or negative in leads from the left side or middle of the chest, and positive in leads from the right side.

The time of onset of excitation in the various precordial leads is shown in Table III. For comparison, the average values of these determinations in normal subjects are included on the lowest line. It is apparent that, in the anterior midthorax, excitation arrives, on the average, at approximately the same time in the normal subject as in the person with dextrocardia. In the latter, the time of arrival on the right side of the precordium is considerably later than on the left side, which is the reverse of what is found in the normal subject.[3] Significant

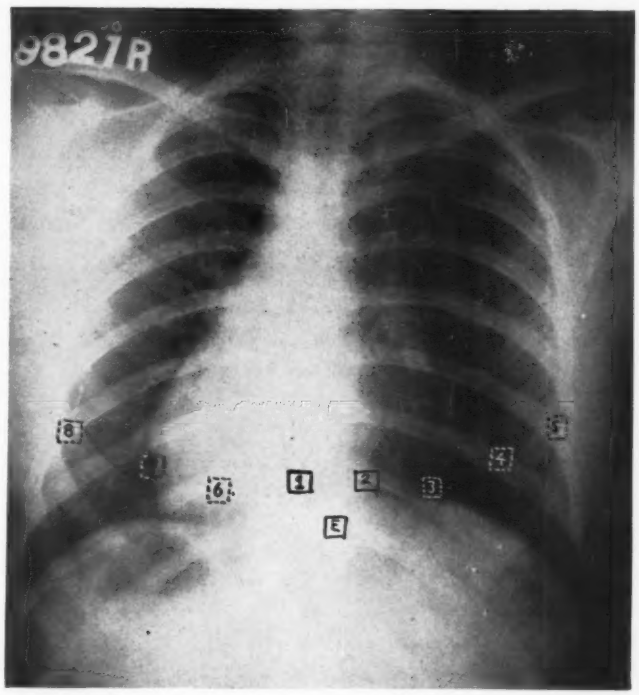



Fig. 3.—Teleroentgenogram in Case 1, showing the approximate location of the thoracic leads with respect to the cardiac silhouette. The relationship of points $V_1$, $V_2$, and $V_E$ was ascertained by placing small lead markers on the chest before the roentgenogram was taken; these points are indicated by squares of solid lines. Other points could not be located accurately in this manner because of prominent breasts. The approximate location of each has been indicated by squares of dotted lines.

differences are noted between average values of Lead $V_6$ in cases of dextrocardia and the comparable Lead $V_3$ of the normal subject, and between the values for Lead $V_E$ in the two groups. A large number of cases would probably reduce these differences. In cases of dextrocardia, the average onset of excitation in the first two leads ($V_1$ and $V_2$) was 0.0160 sec. earlier than the average onset in Leads $V_7$ and $V_8$. The comparable figure in normal subjects, which is the difference

between the average onset in the first two leads and the average onset in the fourth and fifth ($V_4$ and $V_5$), is 0.0164 sec.[3]

## SUMMARY

The results indicate that the electrical field of the heart in cases of dextrocardia is, in effect, a mirror image of the electrical field in the normal subject. That excitation reaches the surface of the thorax near the left ventricle later than it reaches the surface of the thorax near the right ventricle, in the human subject, irrespective of the location of these chambers, may be attributed to factors other than the difference in the thickness of the ventricular walls. The one that comes to mind first is the variation in conductivity of the several components comprising the surrounding medium. At present, there is no direct way of measuring the effect of this on electrical phenomena in the human subject, but the fact that the intrinsicoid deflection is abnormally late in midthoracic leads ($V_1$, $V_2$, $V_E$) in cases of right ventricular hypertrophy and right bundle branch block,[2, 4, 10] and in leads from the left side of the chest in cases of left ventricular hypertrophy and left bundle branch block[2, 4] suggests that, however heterogeneous the conducting medium may be, it has no significant influence.

The author is grateful to Drs. Harry Gold and C. Carusos, of New York, and Drs. Harold Goldberg, Jacob Bleiberg, and Samuel Roth, of Newark, for permission to study their cases.

## REFERENCES

1. Macleod, A. G., Wilson, F. N., and Barker, P. S.: The Form of the Electrocardiogram. I. Intrinsicoid Electrocardiographic Deflections in Animals and Man, Proc. Soc. Exper. Biol. and Med. **27:** 586, 1930.
2. Johnston, F. D., Kossmann, C. E., and Wilson, F. N.: Precordial Leads in Normal Individuals and in Patients with Ventricular Hypertrophy, J. A. M. A. **104:** 147, 1935.
3. Kossmann, C. E., and Johnston, F. D.: The Precordial Electrocardiogram: I. The Potential Variations of the Precordium and of the Extremities in Normal Subjects, Am. Heart J. **10:** 925, 1935.
4. Wilson, F. N., Macleod, A. G., and Barker, P. S.: The Order of Ventricular Excitation in Human Bundle-Branch Block, Am. Heart J. **3:** 305, 1932.
5. Kossmann, C. E., and Rader, B.: The Effect of Potential Variations of the Distant Electrode on the Precordial Electrocardiogram, Am. Heart J. **12:** 698, 1936.
6. Wilson, F. N., Johnston, F. D., Macleod, A. G., and Barker, P. S.: Electrocardiograms That Represent the Potential Variations of a Single Electrode, Am. Heart J. **9:** 447, 1934.
7. Standardization of Precordial Leads, Am. Heart J. **15:** 107 and 235, 1938.
8. Carter, E. P., Richter, C. P., and Greene, C. H.: A Graphic Application of the Principle of the Equilateral Triangle for Determining the Direction of the Electrical Axis of the Heart in the Human Electrocardiogram, Bull. Johns Hopkins Hosp. **30:** 162, 1919.
9. Wilson, F. N., Macleod, A. G., and Barker, P. S.: The T Deflection of the Electrocardiogram, Trans. Assoc. Am. Phy. **46:** 29, 1931.
10. Wilson, F. N., Johnston, F. D., Hill, I. G. W., Macleod, A. G., and Barker, P. S.: The Significance of Electrocardiograms Characterized by an Abnormally Long QRS Interval and by Broad S Deflections in Lead I. Am. Heart J. **9:** 459, 1934.

# THE TOXICITY OF DIGITALIS AND OUABAIN IN ANIMALS UNDER SODIUM THIOPENTOBARBITAL AND SODIUM PENTOBARBITAL ANESTHESIA*

CHARLES M. GRUBER, M.D., PH.D., VICTOR G. HAURY, M.D., AND MILES E. DRAKE, PH.D.
PHILADELPHIA, PA.

ROWE[1] considered dogs unsatisfactory for digitalis assay. Using morphine-ether anesthesia, Haskell, Copenhaver, Stone, and Yost[2] experimented upon seventy-six dogs in an effort to ascertain whether or not they are suitable for the bio-assay of digitalis. They found that the lethal dose varied from 76.3 to 241 mg. per kilogram of body weight, and, consequently, they decided that dogs were less satisfactory than cats for this work. The average lethal dose in their series was 141 mg. of digitalis per kilogram of body weight. The wide range of the lethal dose was to be accounted for, they believed, by variations in the size and the age of the animals used.

Additional studies on the standardization of digitalis, using dogs, were made by McGuigan and McGuigan,[3] who anesthetized the animals by injecting sodium pentobarbital in doses of 35 mg. per kilogram intraperitoneally. The tincture of digitalis was injected intravenously in doses of 0.1 c.c. per kilogram of body weight every five minutes until the animal died. Their tincture was prepared from U.S.P. reference powder, as directed in the United States Pharmacopoeia XI, and, consequently, they say that their tinctures were made to contain 0.1 gram of the international powder in each cubic centimeter. Twenty-one dogs were used, and the average lethal dose was found to be 123 mg. per kilogram. These results checked within 10 per cent of the actual strength of the drug when any two animals were compared. They also ascertained the amount of ouabain, per kilogram of body weight, which was necessary to kill the animals. The average lethal dose of ouabain was found to be 0.104 mg. (0.092 mg. of water-free ouabain) per kilogram of body weight.

That anesthetic doses of thiopentobarbital can cause temporary cardiac irregularities in experimental animals which are not similarly affected by pentobarbital has been reported by a number of observers.[4, 5] This cardiac arrhythmia could be made to disappear by lowering the arterial blood pressure by hemorrhage, and by the administration of such drugs as amyl nitrite, nitroglycerine, and the salts of acetylcholine, histamine, or quinidine. If this irregularity was absent during and immediately after administering anesthetic doses of thiopentobarbital intravenously, it could be induced by elevating the arterial blood pres-

From the Department of Pharmacology, Jefferson Medical College, Philadelphia, Pa.
*This research was made possible through a grant by Parke, Davis and Company to the Department of Pharmacology for research in science.
Received for publication Jan. 18, 1940.

sure by eliminating the carotid sinus reflex, and by the intravenous injection of ouabain, tyramine, ephedrine, or pitressin. In a few instances, epinephrine also induced the irregularity.[6]

Since pentobarbital was the anesthetic used by McGuigan and McGuigan in their studies of the toxicity of digitalis, we thought that it would be interesting to perform similar experiments, with sodium thiopentobarbital (pentothal) as the anesthetic agent, and compare our results with theirs. Such experiments, we believe, are of importance, for both sodium thiopentobarbital and digitalis are used clinically.

## METHOD

Forty-four dogs were used in this investigation; seventeen were under sodium pentobarbital anesthesia, and twenty-seven under sodium thiopentobarbital anesthesia. In one group of experiments ether anesthesia was used for the preliminary operative procedures, after which one or the other of the above-mentioned anesthetics was administered intravenously. In a second group of experiments sodium pentobarbital was injected intraperitoneally, and, in a third series of experiments, sodium thiopentobarbital was injected intravenously in anesthetic doses.

After the animal was anesthetized, the trachea was exposed and cannulated to permit freer breathing and the use of artificial respiration when needed. The right carotid artery was freed and cannulated for recording the arterial blood pressure with a mercury manometer. Heparin was used as the anticoagulant. A small area on the left hind leg, and another similar area on the right foreleg were shaved, and German silver electrodes were applied to these spots. These electrodes were connected to a "Sanborn" string galvanometer.* Lead II was used throughout, and the string tension was adjusted to give an excursion of 2 cm. for each mv. The resistance was 2000 ohms. A commercial paste was employed to reduce skin resistance and to insure better contact between the electrodes and the skin.

The right femoral vein was exposed for the intravenous administration of the drugs. In these experiments, after completion of the operative procedures, electrocardiograms and blood pressure records were taken simultaneously. In those experiments in which ether was used, it was discontinued at this point, and, as the anesthesia became lighter, 20 mg. per kilogram of either sodium thiopentobarbital or sodium pentobarbital were slowly injected intravenously. When thiopentobarbital was used, additional electrocardiograms were taken after its administration, and after each injection of digitalis or of ouabain.

In some experiments, an electrocardiogram was taken as soon as the animal was fastened to an animal board. After this, 20 mg. per kilogram of sodium thiopentobarbital were injected into the saphenous vein. If this amount of thiopentobarbital was insufficient to produce surgical anesthesia, additional amounts were injected. The operative procedures were performed under this anesthetic in these experiments. As the animal recovered from the initial dose of thiopentobarbital, the drug was again injected in doses of 3 to 10 mg. per kilogram, i.e., in doses just sufficient to maintain surgical anesthesia.

In the experiments in which sodium pentobarbital was employed as the anesthetic, the drug was injected intraperitoneally in doses of 35 mg. per kilogram. No electrocardiographic studies were made on these animals.

Two tinctures of digitalis were used. In four experiments the "Wellcome" tincture was employed, but for the thirty-two remaining experiments the tincture was prepared from the United States Pharmacopoeial reference powder, as directed in the U.S.P. XI.

*We wish to thank Dr. Henry K. Mohler, of the Department of Therapeutics, for the use of the string galvanometer employed in this research.

The digitalis was injected intravenously in doses of 0.1 c.c. per kilogram, and from one to three minutes were required for each injection. An attempt was made to keep the injection time at two minutes in every instance. The injection was repeated every five minutes until the animal died. In a few instances in which respiration ceased, artificial respiration was employed.

A 1:10,000 aqueous solution of ouabain (Merck) was used. This concentration was estimated on the basis of water-free ouabain. The theoretical lethal dose for the animal was calculated by using the lethal dose (0.092 mg. per kilogram) established by McGuigan and McGuigan.[3] This dose was divided into twelve parts, and one of these parts (0.00766 mg. per kilogram) was injected intravenously every five minutes until the animal died.

In a few additional experiments, two or four injections of digitalis (0.1 c.c. per kilogram) were made before the administration of sodium thiopentobarbital, while the dog was still under ether anesthesia. The ether was then discontinued, and the animal was given as much thiopentobarbital as was needed to maintain surgical anesthesia.

A kymograph was employed to record the fluctuations in blood pressure and gross changes in cardiac activity. A chronometer which marked intervals of six seconds was placed at the zero blood pressure level. In most of our experiments, simultaneous recordings of the blood pressure and electrocardiogram were made.

## RESULTS

*Digitalis.*—There was no conspicuous difference in susceptibility to digitalis between those animals which received sodium pentobarbital intraperitoneally as the anesthetic, and those which first received ether by inhalation for the operative work, and later were given sodium pento-

TABLE I

| WEIGHT OF ANIMAL IN KG. | NUMBER OF INJECTIONS | C.C. TINCTURE DIGITALIS INJECTED | MG. PER KG. LETHAL | PER CENT OF THEORETICAL LETHAL DOSE |
|---|---|---|---|---|
| 7.7 | 12 | 9.24 | 120 | 98 |
| 7.0 | 9 | 6.3 | 90 | 73 |
| 13.6 | 9 | 12.15 | 90 | 73 |
| 7.7 | 8 | 6.16 | 80 | 65 |
| 7.7 | 12 | 9.24 | 120 | 98 |
| 9.2 | 7 | 6.44 | 70 | 57 |
| 9.3 | 11 | 10.23 | 110 | 90 |
| 11.8 | 11 | 12.98 | 110 | 90 |
| 10.2 | 13 | 13.26 | 130 | 106 |
| 10.7 | 10 | 10.7 | 100 | 81 |
| 13.9 | 11 | 15.29 | 110 | 90 |
| 7.5 | 11 | 8.25 | 110 | 90 |
| 7.5* | 10 | 7.5 | 100 | 81 |
| 9.5* | 12 | 11.4 | 120 | 98 |
| 11.8* | 10 | 11.8 | 100 | 81 |
| 11.6* | 9 | 10.44 | 90 | 73 |
| 12.7* | 13 | 16.5 | 130 | 106 |
| Average | 10.5 | | 105 | 85 |

Dogs anesthetized with sodium pentobarbital, in a dose of 35 mg. per kilogram, given intraperitoneally, were used in all of these experiments except those marked by asterisks. In the latter experiments ether anesthesia was used for the operative work, after which the ether was discontinued and sodium pentobarbital was injected intravenously in a 5 per cent solution in doses of 20 mg. per kilogram. Tincture of digitalis (0.1 c.c. per kilogram) was injected intravenously every five minutes. Usually, two minutes were used in making the injection.

The theoretical lethal doses were obtained by multiplying the weights of the animals, in kilograms, by the factor 123 mg. (McGuigan and McGuigan[3]). Considering that 1 c.c. of the official tincture is equivalent to 0.1 Gm. of the standard powder, the lethal dose in mg. per kilogram was ascertained.

barbital intravenously (see Table I). In seventeen such experiments on dogs that weighed between 7.0 and 13.9 kilograms, the quantity of tincture of digitalis, made with the United States Pharmacopoeial reference powder, which was necessary to kill the animal varied from 0.7 (70 mg. of standard powder) to 1.3 c.c. (130 mg. of standard powder) per kilogram of body weight, a range of 85.7 per cent. The average lethal dose was 105 mg. per kilogram. This is approximately 15 per cent less than that reported by McGuigan and McGuigan.[3]

The actual lethal doses for the dogs used in our experiments varied from 57 to 106 per cent of the theoretical lethal dose. The latter was calculated by multiplying the weight of the animal, in kilograms, by 123 mg., which was found by McGuigan and McGuigan[3] to be the average lethal dose for their animals.

That sodium thiopentobarbital (pentothal sodium) definitely decreases the resistance of dogs to digitalis is shown in Table II. No great difference in toxicity was noted between the five animals which weighed from 5.9 to 11.4 kg. and received only sodium thiopentobarbital, and the ten animals which weighed from 6 to 13.2 kg. and first received ether by inhalation, and, later, sodium thiopentobarbital. In one of our animals (see Table II, ‡), 40 mg. per kilogram of sodium

TABLE II

| WEIGHT OF ANIMAL IN KG. | NUMBER OF INJECTIONS | C.C. TINCTURE DIGITALIS INJECTED | LETHAL DOSE IN MG. PER KG. | PER CENT OF THEORETICAL LETHAL DOSE |
|---|---|---|---|---|
| 7.7 | 8 | 6.16 | 80 | 65 |
| 7.3 | 8 | 5.84 | 80 | 65 |
| 6.0 | 8 | 4.80 | 80 | 65 |
| 10.0 | 7 | 7.00 | 70 | 57 |
| 12.3 | 9 | 11.07 | 90 | 73 |
| 7.7 | 10 | 7.70 | 100 | 81 |
| 6.8 | 10 | 6.80 | 100 | 81 |
| 13.2 | 8 | 10.56 | 80 | 65 |
| 10.0 | 7 | 7.00 | 70 | 57 |
| 8.6 | 10 | 8.60 | 100 | 81 |
| 11.1* | 10 | 11.1 | 100 | 81 |
| 11.4* | 7 | 7.98 | 70 | 57 |
| 5.9* | 8 | 4.72 | 80 | 65 |
| 8.2*‡ | 12 | 9.84 | 120 | 98 |
| 8.2 | 9 | 8.20 | 90 | 73 |
| 9.1* | 11 | 10.1 | 110 | 90 |
| Average | 8.9 | | 89 | 72 |
| 6.8† | 4 | 2.72 | 40 | |
| 6.0† | 6 | 3.6 | 60 | |
| 14.0† | 7 | 9.8 | 70 | |
| 9.0† | 7 | 6.3 | 70 | |

Sodium thiopentobarbital (sodium pentothal) was used as the anesthetic. In all of these experiments, except those indicated by an asterisk, ether anesthesia was used for the preliminary surgical work, and, after the animal had partially recovered from the ether, sodium thiopentobarbital, in 5 per cent solution, was injected intravenously in doses of 20 mg. per kilogram. In those experiments which are marked with an asterisk, sodium thiopentobarbital, injected intravenously in doses of 20 mg. per kilogram, was the anesthetic. In experiments marked with a †, "Wellcome" tincture of digitalis was used. In all others the tincture of digitalis was made from U.S.P. reference powder, as directed in the U.S.P. XI, and the tincture was injected intravenously in a dose of 0.1 c.c. per kilogram every five minutes, each injection taking approximately two minutes.

thiopentobarbital were required to produce light surgical anesthesia. To maintain this anesthesia, 5 mg. per kilogram of this drug had to be injected intravenously every ten minutes. However, after the second injection of the sodium thiopentobarbital (total, 50 mg. per kilogram), and after the fourth injection of digitalis, artificial respiration had to be maintained for the remainder of the experiment. This was the only animal to which it was necessary to give the full, theoretical, lethal dose of tincture of digitalis, i.e., 120 mg. per kg. of body weight, in order to stop the heart. We found that the lethal dose of the U.S.P reference tincture varied from 70 to 120 mg. per kilogram (standard powder), with an average of 89 mg. per kilogram. This average dose is 16 mg. per kilogram less than that in the experiments in which we used pentobarbital as the anesthetic, 34 mg. per kilogram less than that reported by McGuigan and McGuigan,[3] who used pentobarbital anesthesia, and 52 mg. per kilogram less than that (141 mg.) reported by Haskell et al.,[2] who employed morphine-ether anesthesia. The average number of injections of digitalis was 8.9, and the average dose injected was 72 per cent of the average lethal dose reported by other investigators.[3]

In the four experiments, performed on as many dogs, in which "Wellcome" tincture of digitalis was used, the average number of injections was six, and the average dose was but 50 per cent of the theoretical lethal dose, i.e., 60 mg. of standard powder per kilogram of body weight (see Table II). Although these experiments were few, the results compare favorably with those which we obtained when we used a tincture made from U.S.P. reference powder according to the directions given in the United States Pharmacopoeia XI.

Fig. 1 shows results that are typical of all of the experiments in which either tincture of digitalis made from the official reference powder or the commercial tincture was used. The records in this figure were obtained from a 6-kilogram dog which was anesthetized with ether, by inhalation, for operative purposes. After this was completed the ether was discontinued, and, after the anesthesia became light, 10 mg. per kilogram of sodium thiopentobarbital were injected intravenously between the arrows ↑↓ at *2*. To maintain surgical anesthesia, a second injection of 10 mg. per kilogram was made 16 minutes later, between the arrows ↑↓ at *10*. A commercial tincture of digitalis ("Wellcome"), in the amount of 0.1 c.c. per kilogram of body weight, was slowly injected intravenously at *4*, *6*, *8*, *12*, *14*, and *16*. The electrocardiograms below the kymograph record were taken at *3*, *5*, *7*, *9*, *11*, *13*, *15*, *17*, and *18*, as indicated in the kymograph record by corresponding numbers. As a result of the injections of thiopentobarbital and digitalis, the blood pressure increased from 123 to 206 mm. of mercury. Following the sixth injection of tincture of digitalis, the heart abruptly began to fibrillate, the blood pressure dropped to the level of atmospheric pressure, and the respirations became accelerated and finally ceased.

As is usually the case when the arterial blood pressure is low (120 mm. of mercury), no irregularity in the heartbeat occurred after the first injection of the sodium thiopentobarbital. Whether the subsequent irregularity (electrocardiogram 11) was caused by the thiopentobarbital or the digitalis we are unable to say, for these two drugs cause similar irregularities. When thiopentobarbital anesthesia was used, we were unable to ascertain what dose of either digitalis or ouabain was

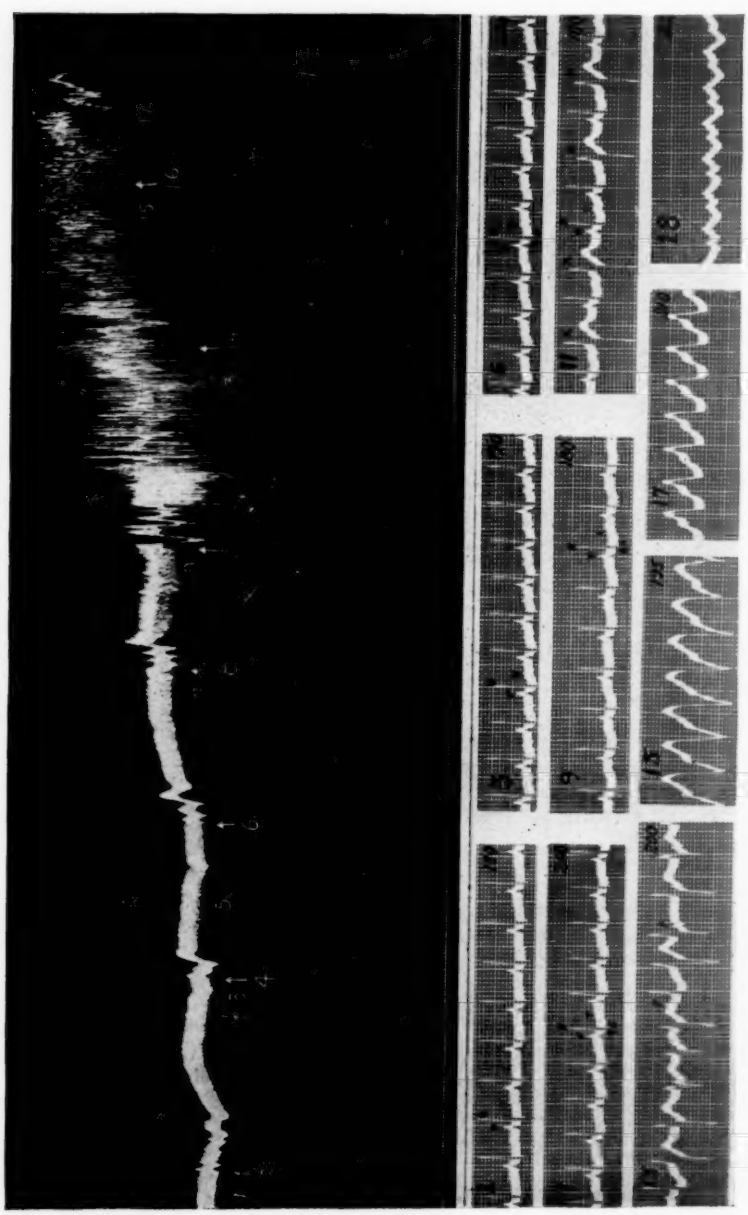


FIG. 1.—Weight of dog, 6 kilograms. Top record is that of the arterial blood pressure, measured with a mercury manometer; below it are the time in intervals of six seconds and zero blood pressure. The numbers to the left in each electrocardiogram correspond to a similar number in the kymographic record itself; the two records were written simultaneously. The numbers to the right of each section of the electrocardiogram indicate the heart rate per minute. For full detail, see text. Record reduced about one-half.

necessary to cause cardiac irregularity because of the fact that the anesthetic itself produced irregularities (premature ventricular contractions) in nineteen of the twenty-seven experiments (see Fig. 2). In one of the experiments in which sodium pentobarbital was used as the anesthetic agent, premature ventricular contractions occurred occasionally. Whether or not they were caused by the anesthetic we do not know. In the remaining sixteen experiments, cardiac irregularity oc-

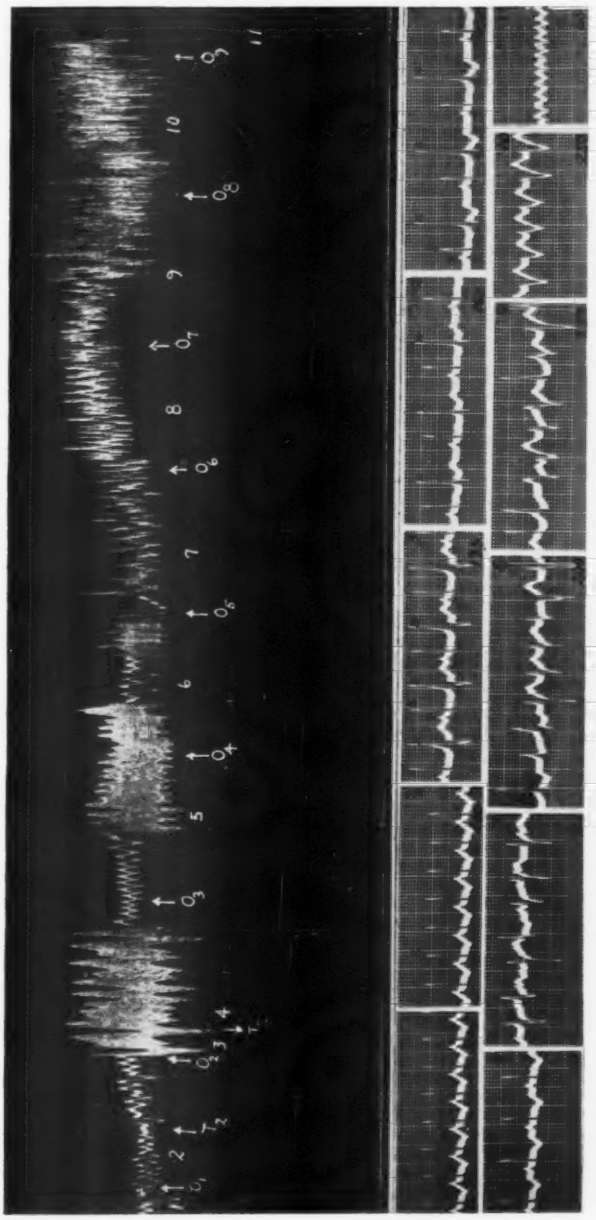


Fig. 2.—Dog, weight 11 kg. Twenty mg. per kilogram of sodium thiopentobarbital were injected intravenously to induce anesthesia. Top record is that of the blood pressure, measured with a mercury manometer, and below this are the time in intervals of six seconds and zero blood pressure. Below the kymograph record there is a series of electrocardiograms. The number in the upper right-hand corner of each segment corresponds to the number in the kymograph record; the two records were taken simultaneously. The numbers in the lower right-hand corners indicate the heart rate per minute. Between the arrows ↑ ↓ at $T_2$, sodium thiopentobarbital, in the amount of 10 mg. per kilogram, was injected intravenously. Ouabain, in a dose of 0.85 c.c. of a 1:10,000 solution, was injected intravenously at $O_1$, $O_2$, $O_3$, etc. During the injection of ouabain at $O_8$, the heart suddenly began to fibrillate, as shown in electrocardiogram 11. Record reduced about one-half.

curred between the fifth and the tenth injections of digitalis. Our average for the entire series of animals was 6.6 injections of 0.1 c.c. per kilogram of tincture of digitalis.

TABLE III

| WEIGHT OF ANIMAL IN KG. | NUMBER OF INJECTIONS | LETHAL DOSE IN MG. | LETHAL DOSE IN MG. PER KG. | LETHAL DOSE IN PER CENT OF THEORETICAL LETHAL DOSE |
|---|---|---|---|---|
| 16.8 | 7 | 0.90 | 0.054 | 59 |
| 11.0 | 8 | 0.67 | 0.062 | 67 |
| 11.8 | 8 | 0.72 | 0.061 | 66 |
| 11.8 | 6 | 0.54 | 0.046 | 50 |
| 13.4 | 9 | 0.92 | 0.069 | 75 |
| 7.0 | 8 | 0.43 | 0.060 | 67 |
| 7.7 | 5 | 0.30 | 0.039 | 42 |

The toxicity of ouabain in dogs under sodium thiopentobarbital anesthesia (pentothal sodium). The drug was injected intravenously in a 1:10,000 solution, and each dose contained 0.00766 mg. of ouabain per kilogram of body weight. The theoretical lethal dose was calculated by multiplying the weight of the animal, in kilograms, by 0.092 mg. (McGuigan and McGuigan.)

*Ouabain.*—The results of our experiments with ouabain support our observations on digitalis (see Table III). The number of injections of ouabain (1:10,000 solution) varied from six to nine, and the amount injected ranged from 0.039 to 0.069 mg. per kilogram of body weight. The average lethal dose was found to be 0.056 mg. per kilogram. This is 39 per cent less than the calculated lethal dose. The latter was estimated by multiplying the weight of the animal, in kilograms, by 0.092 mg., which was the average lethal dose in McGuigan and McGuigan's experiments. In our experiments the lethal dose was 25 to 58 per cent less than that reported by other investigators who used pentobarbital as the anesthetic.[3]

Only one record is presented to illustrate the effects of ouabain, for it is fairly representative of all the experiments. The records in Fig. 2 were obtained from an 11 kg. dog which was given sodium thiopentobarbital in a dose of 20 mg. per kilogram, intravenously, for operative purposes. A second intravenous injection of sodium thiopentobarbital, in the amount of 10 mg. per kilogram, was made between the arrows ↑↓ at $T_2$ as indicated in the kymograph record. We are aware of the possibility that a second injection of sodium thiopentobarbital may be followed by sudden failure of the heart,[7] but in this and other similar experiments this did not occur. After completion of the operation the blood pressure was recorded and electrocardiogram 1 was taken, at 1, as indicated in the kymograph record. At $O_1$, $O_2$, $O_3$, etc., 0.85 c.c. of a 1:10,000 solution of ouabain was injected intravenously, and electrocardiograms were taken approximately two to two and one-half minutes after each injection. These electrocardiograms show that, at first, the heart rate decreased gradually from 204 to 140 beats per minute. Following this decrease, the heart accelerated to 220 beats per minute, and, finally, the ventricle began to fibrillate at a rate of 550 waves per

minute. The blood pressure gradually increased from 144 to 192 mm. of mercury. When the ninth injection of ouabain was about half finished, the heart suddenly began to fibrillate, and the blood pressure dropped to the atmospheric pressure level. Inasmuch as the animal died during this last injection of ouabain, the sum of eight injections was regarded as the lethal dose. The second injection of pentothal sodium was accompanied, as was the first, by premature ventricular contraction (see electrocardiograms 3 and 4).

*Blood Pressure.*—Not only did pentobarbital and thiopentobarbital modify the effects of digitalis and of ouabain on the heart muscle proper, but, apparently, they also influenced the general arterial blood pressure in a similar manner. When sodium pentobarbital was used as the anesthetic, the control blood pressures in this series averaged 152 mm. of mercury (see Table IV). This was increased by the injections of

TABLE IV

THE EFFECT ON THE ARTERIAL BLOOD PRESSURES IN DOGS UNDER PENTOBARBITAL, ETHER-THIOPENTOBARBITAL, AND THIOPENTOBARBITAL ANESTHESIA OF INJECTING DIGITALIS AND OUABAIN INTRAVENOUSLY

| DRUG | ANESTHETIC | EXTREMES IN CONTROL BLOOD PRESSURE | AVERAGE CONTROL BLOOD PRESSURE | EXTREMES IN MAXIMUM BLOOD PRESSURE | AVERAGE MAXIMUM BLOOD PRESSURE | EXTREMES IN BLOOD PRESSURE BEFORE CARDIAC FAILURE | AVERAGE BLOOD PRESSURE BEFORE CARDIAC FAILURE |
|---|---|---|---|---|---|---|---|
| Digitalis | Pentobarbital | 110-178 | 152 | 140-211 | 179 | 62-186 | 131 |
| Digitalis | Ether and Thiopentobarbital | 114-160 | 140 | 160-270 | 202 | 80-250 | 142 |
| Digitalis | Thiopentobarbital | 147-190 | 169 | 174-240 | 203 | 102-185 | 146 |
| Ouabain | Ether and Thiopentobarbital | 120-164 | 141 | 140-230 | 199 | 90-210 | 160 |

digitalis to an average of 179 mm. In these animals, just before the heart began to fibrillate, the average blood pressure was 131 mm. In those experiments in which thiopentobarbital was used after ether had been employed for operative purposes, the control blood pressures, while the animals were under ether anesthesia, averaged 140 mm. of mercury (see Table IV). After withdrawal of the ether anesthesia and following the injection of thiopentobarbital and digitalis, the maximum pressures averaged 202 mm. Just before the heart either ceased beating or began to fibrillate, these general blood pressures averaged 142 mm. In those experiments in which ouabain was used, and those in which sodium thiopentobarbital was the sole anesthetic agent, the average control blood pressures were 141 and 169 mm. of mercury, respectively. These averages were increased to a maximum of 199 mm. Hg, in the former, by ouabain and thiopentobarbital, and, in the latter, to 203 mm. Hg by the thiopentobarbital and digitalis. Just before the heart ceased

beating or began to fibrillate, these average pressures were 160 and 146 mm. of mercury, respectively (see Table IV). It will be noted that the blood pressure reached a higher maximum in all of the experiments in which thiopentobarbital was used as the anesthetic agent.

There were two experiments in which two injections of tincture of digitalis were made while the animals were under ether anesthesia, and two experiments in which four injections were given. In each experiment, after the last injection of digitalis, the ether was discontinued, and sodium thiopentobarbital, in the amount of 20 mg. per kilogram, was injected slowly intravenously. In all four experiments the second injection of thiopentobarbital (10 mg. per kilogram) caused sudden cardiac arrest. In all of these experiments the first injection of pentothal sodium was accompanied by premature ventricular contractions.

## DISCUSSION

Judging from our results and those of other investigators, it appears that dogs are not good animals to use for the bio-assay of digitalis. Although we attempted, whenever possible, to maintain identical conditions in all of our experiments (except for weight and age of animals, and these were restricted to a narrow range), nevertheless the lethal dose of digitalis varied more than 85 per cent in dogs under pentobarbital anesthesia. A similar variation in response to digitalis was noted in those of our experiments in which thiopentobarbital was used as the anesthetic agent.

In comparing our results on animals under pentobarbital and thiopentobarbital anesthesia, it is evident that the toxic effect of thiopentobarbital on the heart simply adds to the toxicity of both digitalis and ouabain. We found that the average lethal dose of digitalis, per kilogram, when the animals were under thiopentobarbital anesthesia, was 16 mg. less than that for animals under pentobarbital anesthesia. If these results are compared with those of McGuigan and McGuigan,[3] the difference becomes 34 mg. per kilogram less. Similarly, when the average lethal dose of ouabain for the dogs under thiopentobarbital anesthesia is compared with that reported by the above investigators, it is found that our animals required 39 per cent less ouabain per kilogram.

Our studies on blood pressure support the view that it may make some difference, with respect to the action of digitalis and ouabain, whether one uses pentobarbital or thiopentobarbital anesthesia. The average maximum blood pressures after the injection of either tincture of digitalis or ouabain were 20 mm. of mercury higher in the animals under thiopentobarbital anesthesia.

The difference between the toxic effect of digitalis and ouabain on dogs under thiopentobarbital (pentothal) anesthesia and dogs under pentobarbital anesthesia is to be attributed, we believe, to the toxic action of pentothal on cardiac muscle. Of the seventy-nine dogs which

received sodium thiopentobarbital, a cardiac irregularity (premature ventricular contractions) occurred either during, or immediately after, the completion of the injection in fifty-five, an incidence of over 69 per cent. If we include, also, those injections which were made to maintain anesthesia, we find that premature ventricular contractions were noted after 105 of the 143 injections (73 per cent).

## SUMMARY

1. Dogs are not satisfactory animals for the bio-assay of digitalis.

2. Anesthetic agents play a rôle in determining the toxicity of digitalis and ouabain. When sodium thiopentobarbital is used the amounts of either digitalis or ouabain which are needed to bring about cessation of cardiac activity are much less than those required when sodium pentobarbital is the anesthetic agent.

## REFERENCES

1. Rowe, L. W.: Digitalis Standardization, A Consideration of Certain Methods of Biological Assay, J. Am. Pharm. A. **8**: 900, 1919.
2. Haskell, C. C., Copenhaver, J. R., Stone, G. E., and Yost, O. R.: The Use of Dogs in the Assay of Digitalis. A Comparison With the Results Obtained on Cats, J. Lab. and Clin. Med. **14**: 155, 1928.
3. McGuigan, R. A., and McGuigan, H. A.: The Use of Dogs for the Standardization of Digitalis, J. Pharmacol. and Exper. Therap. **63**: 76, 1938.
4. Gruber, C. M.: On Certain Pharmacologic Actions of the Newer Barbituric Acid Compounds, Am. J. Obst. and Gyn. **33**: 729, 1937; The Effects of Anesthetic Doses of Sodium Thiopentobarbital, Sodium Thioethyamyl and Pentothal Sodium Upon the Respiratory System, the Heart and Blood Pressure in Experimental Animals, J. Pharmacol. and Exper. Therap. **60**: 143, 1937.
5. Kohn, R., and Lederer, L.: Pentothal Studies With Special Reference to the Electrocardiogram, J. Lab. and Clin. Med. **23**: 717, 1938.
6. Gruber, C. M., Haury, V. G., and Gruber, C. M., Jr.: The Cardiac Arrhythmia, Characteristic Effect of the Thiobarbiturates, as Influenced by Changes in Arterial Blood Pressure, J. Pharmacol. and Exper. Therap. **63**: 193, 1938.
7. Veal, J. R., and Reynolds, C.: The Cumulative Effects of Pentothal Sodium, South. Med. J. **31**: 649, 1938; Reynolds, C., and Veal, J. R.: Circulatory Versus Respiratory Deaths from Pentothal Sodium, South. Med. J. **31**: 650, 1938; Reynolds, C.: Dangers of Prolonged Pentothal Sodium Anesthesia from the Pharmacological Standpoint, Anesth. and Analg. **18**: 270, 1939.

# THE INCIDENCE OF SYPHILITIC AORTITIS IN A REPRESENTATIVE MUNICIPAL HOSPITAL

ABRAHAM GELPERIN, M.D.
CINCINNATI, OHIO

THE incidence of syphilis has been shown to be greatest in the lower economic strata of society.[1, 2, 3, 4, 5] Turner,[6] in a study of 10,000 consecutive cases of syphilis, found that a diagnosis of cardiovascular syphilis had been made in 10.1 per cent of the cases of late syphilis. Bruusgaard[7] followed 473 patients who had received no treatment for their early syphilis, and found that 12.8 per cent developed cardiovascular syphilis. It is logical to assume, therefore, that syphilis of the cardiovascular system would constitute a major medical problem in hospitals (city, county, or state) which furnish medical care to those in the lowest economic groups. Since, in all cases, syphilitic valvulitis and aneurysm evolve from a pre-existing syphilitic aortitis, the present study has been undertaken in an attempt to ascertain the incidence of syphilitic aortitis in the wards of the Cincinnati General Hospital.

This hospital has 925 beds, and serves the low-income groups of the population of Cincinnati. For over ten years, less than 10 per cent of the patients who were admitted were able to pay even a small portion of the cost of hospitalization. Negroes constitute approximately 35 per cent of the total number of patients who are admitted each year.

Only cases in which a histologic diagnosis of syphilitic aortitis had been made by members of the Department of Pathology were included in this study. All such cases which were encountered between 1926 and 1937, inclusive, were reviewed. Cases in which the aortitis was accompanied by aneurysm, valvulitis, or gumma were omitted from consideration.* Table I shows the incidence of these cases.

Statistical conclusions drawn from autopsy material must be qualified before they can be applied to a living population. The following paragraphs discuss the variants encountered in this study:

Cases which were encountered in a sample period (1936 to 1937) were studied in detail in order to ascertain the age incidence at death and autopsy, as well as the number of patients with syphilitic aortitis who had had antisyphilitic therapy. Of the 138 patients who were studied, twenty-seven had had some antisyphilitic treatment, but only seven had had what may be considered sufficient therapy. The remaining patients were either too ill on admission for specific questioning, gave a history of untreated syphilis, or denied any knowledge of infection. As is shown in Table II, the mortality among the young and those over 40 was higher

From the Cincinnati Department of Health and the Department of Internal Medicine, University of Cincinnati School of Medicine, Cincinnati, Ohio.

Received for publication Jan. 10, 1940.

*I wish to thank Dr. Richard S. Austin, Director of the Department of Pathology, for permission to study this autopsy material, and for his generous counsel.

TABLE I

HOSPITAL STATISTICS RELATIVE TO SYPHILITIC AORTITIS FOR THE YEARS 1926 TO 1937, INCLUSIVE

| YEAR | HOSPITAL ADMISSIONS | DEATHS | AUTOPSIES | NO. CASES OF SYPHILITIC AORTITIS* | APPROXIMATE NUMBER OF CASES OF SYPHILITIC AORTITIS PER ANNUM |
|---|---|---|---|---|---|
| 1926 | 11,518 | 1,273 | 422 | 31 (7.3%) | 841 |
| 1927 | 12,177 | 1,253 | 483 | 37 (7.6%) | 925 |
| 1928 | 13,086 | 1,374 | 553 | 39 (7.1%) | 929 |
| 1929 | 13,832 | 1,530 | 664 | 79 (10.4%) | 1,435 |
| 1930 | 14,580 | 1,491 | 644 | 68 (10.5%) | 1,531 |
| 1931 | 15,172 | 1,554 | 572 | 76 (13.2%) | 2,003 |
| 1932 | 16,116 | 1,555 | 676 | 53 (7.8%) | 1,257 |
| 1933 | 16,777 | 1,587 | 675 | 53 (7.8%) | 1,309 |
| 1934 | 16,903 | 1,785 | 734 | 54 (7.3%) | 1,234 |
| 1935 | 16,234 | 1,679 | 618 | 72 (11.5%) | 1,867 |
| 1936 | 16,629 | 1,702 | 813 | 74 (9.1%) | 1,533 |
| 1937 | 15,834 | 1,611 | 830 | 64 (7.7%) | 1,219 |

*Diagnosis made at autopsy; uncomplicated by aneurysm, valvulitis, or gumma.

TABLE II

PERCENTAGE OF DEATHS (FROM ALL CAUSES) AND AUTOPSIES OCCURRING IN VARIOUS AGE GROUPS DURING THE SAMPLE YEARS 1936 AND 1937

| AGE GROUP | PER CENT OF TOTAL DEATHS (3313) DURING 1936 AND 1937 | PER CENT OF TOTAL AUTOPSIES (1643) DURING 1936 AND 1937 |
|---|---|---|
| 0–19 | 24.7% | 23.0% |
| 20–39 | 18.6% | 14.4% |
| 40–59 | 28.0% | 30.3% |
| 60–up | 28.7% | 32.3% |

than between the ages of 20 and 39, although the per cent of autopsies for each age group was roughly proportional to the per cent of deaths in that group. Because syphilitic aortitis almost never occurs in children,[8, 9] they merely act as a statistical diluent. Also, a preponderance of the aged does not detract from the value of this study, for the majority of syphilitic infections are acquired during the second and third decades of life[10, 11]; therefore, microscopic evidence of syphilis in patients over 40 is an indication of an infection which was probably acquired earlier in life. This fact tends to compensate for the lower death rate among adults under 40.

There is a widespread assumption that it is comparatively easy to obtain permission for a post-mortem examination from relatives of colored patients. However, a comparison of the number of negroes admitted to the hospital (approximately 35.0 per cent) with the percentage of negroes autopsied (39.6 per cent), for the years 1936 and 1937, shows only a 4.6 per cent difference in this respect.

It is acknowledged that routine section and microscopic examination of the aorta will unavoidably miss an unestimated number of actual

lesions. Not only is syphilitic involvement of the cardiovascular system focal in character, but sections are not always taken routinely from all grossly abnormal areas.

An autopsy group is, in itself, not an entirely fair sample of the population. The patients were not only hospitalized for one reason or another, but they did not survive.

Among the variants which have been discussed, there are two which make for an underestimation of the incidence of syphilitic aortitis, namely, (1) the fact that the patients in one group were less than 20 years old, and (2) that there must have been a number of patients with unrecognized syphilitic aortitis.

On the other hand, syphilitic aortitis is supposed to have a detrimental effect on the ability of a patient to combat another disease. The modifying action of syphilitic aortitis upon the death rate from infections and diseases of senescence has not yet been ascertained. Vonderlehr[12] has calculated that syphilis reduces the life expectancy 17.0 per cent (4.8 years) for a white man of 30, and 30.5 per cent (7.1 years) for a negro 30 years of age. McDaniel,[5] in a study of people on the relief rolls of Fulton County, Georgia, found that syphilis constitutes a definite economic handicap; 17 per cent of those between the ages of 20 and 40 were partially incapacitated, and 16 per cent of those over 50 were totally incapacitated. These factors tend to neutralize the variants discussed in the previous paragraph. The exact degree of neutralization cannot be ascertained; nevertheless, it is considered that the application of the data derived from the autopsy material to the general population will give reasonably accurate information—at least to the important extent of determining whether the yearly incidence of syphilitic aortitis is approximately 1000, or 100.

Of the 7,683 autopsies which were performed between 1926 and 1937, inclusive, microscopic evidence of syphilitic aortitis (excluding all developmental complications) was found in 700, or 9.1 per cent.

Lamb,[13] in a survey of the post-mortem material at the Presbyterian Hospital, New York, found that the incidence of syphilitic aortitis, per se, was 5.1 per cent. Welty,[14] at the Philadelphia General Hospital, found that the incidence of syphilitic aortitis, excluding aneurysm and valvulitis, was only 4.2 per cent in a large post-mortem group in which negroes formed 40 per cent of the total. Carr[15] collected eighty-three cases of syphilitic aortitis, per se, from a series of 955 autopsies[16] which were performed in 1929 at the Cook County Hospital, an incidence of 8.7 per cent. Such variations in the incidence of syphilitic aortitis in autopsy groups depend, in great measure, on differences in the social status of the source population, and on the number of negroes who are included.

It is to be expected that approximately 8 per cent of the white, and 25 per cent of the negro, patients in a hospital that cares for the indigent

sick will have syphilis.[2, 5, 17, 18] If the above percentages are applied to the autopsy group herein studied, the calculation shows that there should be 1,132 patients with syphilis (14.6 per cent). Since not all patients with syphilis have syphilitic aortitis, and estimations of its incidence vary from 50 to 90 per cent,[19, 20, 21] if we apply an average figure of 70 per cent to our post-mortem material we should have 792 cases of syphilitic aortitis, or 10.3 per cent. This predicted percentage is comparable to the actual incidence, which was 9.1 per cent.

Judging from the calculated incidence of syphilitic aortitis, column 6, of Table I, indicates approximately the number of patients with syphilitic aortitis who were admitted to the Cincinnati General Hospital during each year of the period between 1926 and 1937, inclusive.

## DISCUSSION

It has been calculated that at least 1,200 patients with syphilitic aortitis are admitted to the Cincinnati General Hospital each year, which means that the hospital has a larger number of cases of this disease than of any other. This brings up the problem of diagnosis and treatment. Since the latter has been amply reviewed, it will not be considered here. However, the diagnosis of syphilitic aortitis, uncomplicated by its late developmental complications, would seem to merit more practical consideration than it has yet received.

The clinical diagnosis of "uncomplicated syphilitic aortitis" has been discussed by Moore,[22] but the validity of such a diagnosis has not been absolutely established.[23, 24] It would seem that, for practical purposes, and because of the large number of cases involved, the problem might be solved by a better application of our knowledge of the pathology of syphilis. Except during the relatively short, early, mucocutaneous infectious, and late visceral, stages, syphilis in its latent period is not moribund, but smoldering, and is slowly but surely destroying irreplaceable vital tissue.[12, 19] We are unable to predict who will develop, and who will escape, the disastrous developmental complications of syphilitic aortitis. Therefore, it is suggested that "probable syphilitic aortitis" be added to each diagnosis of late, latent syphilis.

## SUMMARY

1. A study of the autopsies performed at the Cincinnati General Hospital from 1926 to 1937, inclusive, revealed that the average incidence of syphilitic aortitis (excluding all developmental complications) was 9.1 per cent.

2. At least 1,200 patients with syphilitic aortitis are admitted to the Cincinnati General Hospital each year.

3. It is suggested that each patient with late, latent syphilis, who has not had adequate specific treatment, should be considered as having active syphilitic aortitis.

REFERENCES

1. Parran, T., Jr.: Syphilis From the Epidemiologist's Point of View, Am. J. Pub. Health **22**: 141, 1932.
2. Gould, S. E.: Age Distribution of Syphilis Among Indigent Patients, Am. J. Syph., Gonorr. and Ven. Dis. **20**: 523, 1936.
3. Short, J. J., and Kelley, M. F.: Incidence of Syphilis in General Population and Comparison of Kahn and Wassermann Tests, New Eng. Med. J. **210**: 417, 1934.
4. Diehl, H. S.: Wassermann, Reactions in College Students, Am. J. Pub. Health **21**: 1131, 1931.
5. McDaniel, J. G.: Syphilitic and Nonsyphilitic Persons on Fulton County, Georgia, Relief Rolls, Comparative Study, J. A. M. A. **108**: 1156, 1937.
6. Turner, T. B.: Race and Sex Distribution of Lesions of Syphilis, Bull. Johns Hopkins Hosp. **46**: 159, 1930.
7. Bruusgaard, E.: Über das Shicksal der nicht spezifisch behandelten Luetiker, Arch. f. Derm. u. Syph. **157**: 309, 1929.
8. McDonald, S., Jr.: Syphilitic Aortitis in Young Adults With Specific Reference to a Congenital Etiology, Brit. J. Ven. Dis. **10**: 183, 1934.
9. Given, T. B.: Syphilitic Aortitis in Congenital Syphilis, AM. HEART J. **6**: 132, 1930.
10. Leblanc, T. J.: Venereal Disease Incidence at Different Ages in Certain Southern States, Ven. Dis. Bulletin No. 78, U. S. Public Health Service, 1925.
11. Laurence, J. J., and Tewksbury, R. B.: Incidence of Venereal Diseases at Different Ages, Ven. Dis. Inform. **4**: 435, 1923.
12. Vonderlehr, R. A., and Usilton, L. J.: Syphilis: Chance of Acquisition and the Frequency of Its Disastrous Course, N. Y. State J. Med. **38**: 1376, 1938.
13. Lamb, A. R.: Syphilis of the Cardiovascular System, Nelson's Loose Leaf Med. **4**: 337, 1937.
14. Welty, J. W.: A Necropsy Survey of Cardiovascular Syphilis With Particular Reference to Its Decreasing Incidence, Am. J. Med. Sc. **197**: 782, 1939.
15. Carr, J. G.: Gross Pathology of Heart in Cardiovascular Syphilis, AM. HEART J. **6**: 30, 1930.
16. Kirschbaum, J. D.: Personal communication.
17. Holloway, G. D., Grant, W. H., and Bent, M. J.: Incidence of Syphilis in Negro as Indicated by Serologic Tests, Am. J. Syph., Gonorr. and Ven. Dis. **21**: 303, 1937.
18. Goldblatt, S.: Relation Between Syphilis and Tuberculosis in the Negro, Arch. Derm. and Syph. **40**: 792, 1939.
19. Warthin, A. J.: Role of Syphilis in the Etiology of Angina Pectoris, Coronary Arteriosclerosis, and Thrombosis, and of Sudden Cardiac Death, AM. HEART J. **6**: 163, 1930.
20. Langer, E.: Die Häufigkeit der luetischen Organ-veränderungen insbesondere der Aortitis luetica, München. med. Wchnschr. **73**: 178, 1926.
21. Nickel, H.: Statistische Untersuchungen über die Häufigkeit der Lues am Obduktionsmaterial, Klin. Wchnschr. **15**: 121, 1936.
22. Moore, J. E., Danglade, J. H., and Reisinger, J. C.: Diagnosis of Syphilitic Aortitis, Uncomplicated by Aortic Regurgitation or Aneurysm. Comparison of Clinical and Necropsy Observations in 105 Patients, Arch. Int. Med. **49**: 753, 1932.
23. Keefer, C. S., and Resnik, W. H.: Paroxysmal Dyspnoea as a Symptom of Syphilitic Aortitis, Arch. Int. Med. **37**: 264, 1926.
24. Wilson, R. W., Jr.: Studies in Syphilitic Cardiovascular Disease. 1. Uncomplicated Syphilitic Aortitis, an Asymptomatic Condition, Am. J. Med. Sc. **194**: 178, 1937.

# THE CARDIOVASCULAR SYSTEM IN PULMONARY TUBERCULOSIS

JOHN A. SWEENEY, M.D.
PHILADELPHIA, PA.

THERE have been some misconceptions concerning the relation of certain types of heart disease to active pulmonary tuberculosis. Mitral stenosis has been considered rare in cases of pulmonary tuberculosis, as also have other forms of chronic valvular heart disease which are frequently associated with chronic passive congestion. These statements were formerly widely accepted, but, in view of our present knowledge, they are not justified.

## CONGESTIVE FAILURE

The difficult problem of differentiating between the congestive failure of heart disease and the manifestations of pulmonary tuberculosis is frequently encountered. The symptoms are often identical, namely, cyanosis, shortness of breath on effort, orthopnea, cough, diminished vital capacity, palpitation, and edema. In cases of primary heart disease, evidence of a rheumatic or syphilitic cardiovascular process is usually obtained from the history, physical examination, and roentgenologic studies. The presence of any of the different types of cardiovascular disease, namely, rheumatic, syphilitic, hypertensive, or arteriosclerotic, may of itself account for the signs above mentioned. However, they may occur in certain instances in association with pulmonary tuberculosis alone, either active or healed.

Clinically, it is possible to differentiate between right- and left-sided heart failure, which is a point of considerable importance, especially when mechanical interference in pulmonary tuberculosis is being considered. The right side of the heart possesses a large physiologic factor of safety which enables it to cope adequately with extensive disease of the pulmonary vascular bed. Left-sided failure is a serious condition, and carries a greater risk. It results from hypertension, aortic valvular disease, or infarction of the left ventricle. These are not common factors in pulmonary tuberculosis.

## CAUSE OF SYMPTOMS

The alteration of the alveolar walls which interferes with adequate areation of the blood in its passage through the lungs gives rise to anoxemia. Reduction in the area of the pulmonary vascular bed, increasing pulmonary peripheral resistance and leading to hypertension of the pulmonary circuit, plays an important role in the genesis of failure of the right side of the heart in chronic pulmonary disease. The other causes of right ventricular strain are mitral stenosis, pulmonic stenosis and insufficiency, pulmonary endarteritis, organic tricuspid in-

Received for publication Jan. 24, 1940.

sufficiency, marked pulmonary fibrosis, and pulmonary emphysema. In pulmonary tuberculosis, the latter two are important causes of cardiac insufficiency.

### CARDIAC INVOLVEMENT IN PULMONARY TUBERCULOSIS

Involvement of the heart in pulmonary tuberculosis may be divided into (1) effects of adhesions upon a normal heart; (2) results of tuberculous pericarditis, and (3) results of tuberculous myocarditis. Before describing other types, it is appropriate to consider cases in which the heart is normal, as it usually is in tuberculosis.

### THE HEART IN TUBERCULOSIS

In cases of pulmonary tuberculosis, the heart is described as being characteristically small because of the fact that it is of the dropped or pendulum type. Some have regarded this as a congenital condition, as a result of which poor circulation in the lungs and elsewhere in the body paves the way for the development of pulmonary tuberculosis, but the fact is that the more vascular tissues are the ones which are susceptible to tuberculosis, not the avascular tissues. Others are of the opinion that it is an acquired abnormality, that the small heart is the result of a tuberculous toxemia, producing wasting, loss of tone, and deterioration of heart muscular tissue, as well as of muscle and other tissue throughout the body. However, the heart in pulmonary tuberculosis bears a normal relation to the body weight.

### TUBERCULOUS PERICARDITIS

Tuberculosis of the heart is by no means rare, although, when one considers the large number of cases of tuberculosis, involvement of the heart is at least infrequent.[1] Tuberculous pericarditis is by far the most frequent and most important form. It occurs in about 1 per cent of all autopsies, and in about 3 per cent of autopsies on tuberculous patients. It has been observed in all decades of life, from the second to the seventh. At the Philadelphia General Hospital it is twice as frequent in the colored race as in the white.

There are three main types of tuberculous pericarditis which are important from the clinical as well as from the pathologic standpoint: (1) So-called primary pericarditis, in which the tuberculous involvement is limited, as far as one can ascertain clinically, to the pericardium. The lungs are free from involvement, as are other parts of the body except the mediastinal nodes. In these cases, the disease not infrequently terminates in generalized miliary tuberculosis. (2) Pericarditis associated with either active or healed tuberculosis of the lung. (3) Pericarditis associated with tuberculosis elsewhere in the body, particularly bone tuberculosis.

### SYMPTOMS OF TUBERCULOUS PERICARDITIS

The symptomatology of this condition varies with the type and degree of involvement. Its presence during the course of active pulmonary tuberculosis may be masked by the symptoms and signs of the pulmonary disease. In a typical case of so-called primary tuberculous pericarditis, the onset is usually insidious, with signs of an upper respiratory infection. Patients complain of lassitude and general weakness, and may have a slight fever for weeks. Precordial pain is not infrequently observed; a friction rub may be audible for long periods of time, and yet the patient may complain of comparatively little discomfort. A patient with tuberculous pericarditis may feel well enough to walk about, but one with rheumatic pericarditis is ill, and confined to bed. The latter is also true of the patient with the pericarditis which occurs in the terminal stages of nephritis. With the development of moderate to marked effusion, evidence of cardiac embarrassment appears. Obvious dyspnea is present only when the effusion is very large. Congestive heart failure is practically never observed except as a terminal event. The bases of the lungs remain surprisingly clear, even when the effusion is very large. In one-third of the cases there is a leucopenia, with a relative neutrophilia, but no typical hematologic changes occur in tuberculous pericarditis.

### THE DIAGNOSIS OF TUBERCULOUS PERICARDITIS

The diagnosis of tuberculous pericarditis must be established both anatomically and etiologically. The clinical features of tuberculous pericarditis differ in no way from those of other forms of pericarditis. There may be an effusion, or a thickened pericardium. The fact that it is tuberculous is relatively easy to establish when the patient has tuberculosis of the lung. In fact, pericarditis which occurs when there is active tuberculosis anywhere in the body is nearly always tuberculous. The chief difficulty in differential diagnosis arises in cases of the so-called chronic, primary type. This must be differentiated from rheumatic pericarditis and that associated with the terminal stage of nephritis. The following points are of help. Rheumatic pericarditis attacks children and young adults who usually present other manifestations of rheumatic fever or carditis. It is rare in later life. Tuberculous pericarditis occurs frequently in the later decades. The incidence of rheumatic pericarditis is no greater in one race than another, whereas two-thirds of the cases of tuberculous pericarditis occur in the colored race. Pain is a very prominent symptom of rheumatic pericarditis, and the patient is quite ill and uncomfortable. Pain may be entirely absent in tuberculous pericarditis. In fact, the patient may appear quite comfortable and be able to walk about, despite the fact that he has a small effusion and a rather loud friction rub over the precordium. There are no joint involvement, no murmurs of cardiac origin, and no associated pulmonary congestion. The effusion is hemorrhagic, and some-

times tubercle bacilli may be recovered from the aspirated material. After aspirating the fluid and injecting air, the heart is found not to be enlarged. Thickening of the pericardium, with calcification, may be present. Generally, the prognosis is poor, although cases are occasionally observed in which the patient recovers from the acute stage, and develops a chronic, adherent process.

TABLE I

DIFFERENTIAL DIAGNOSIS OF TUBERCULOUS AND RHEUMATIC PERICARDITIS

| | TUBERCULOUS PERICARDITIS | RHEUMATIC PERICARDITIS |
|---|---|---|
| Age | Usually occurs in the later decades | Occurs in children or young adults who present other manifestations of rheumatic fever or carditis. Rare in later life |
| Racial predilection | Two-thirds of cases occur in the colored race | None |
| Pain | Often absent | Prominent symptom |
| Activity | Patient may appear comfortable, and walk about | Patient quite ill and confined to bed. |

### TREATMENT OF TUBERCULOUS PERICARDITIS

The treatment of tuberculous pericarditis with effusion consists in withdrawal of the fluid, especially if the effusion is large, and replacing it with air. When it progresses to the adherent or constrictive stage, some other form of operative procedure may be indicated, as advocated by Beck and Griswold.[2]

### OTHER FORMS OF PERICARDITIS

The rheumatic type of pericarditis occurs in association with rheumatic valvular heart disease, most frequently aortic or mitral, or even both. Congestive pulmonary phenomena are usually present. The effusion is serofibrinous and sterile. The heart is enlarged, active rheumatic fever is usually present, and the patient is obviously acutely ill.

The pericarditis which is associated with advanced nephritis rarely offers any difficulty in diagnosis.

### TUBERCULOSIS OF THE MYOCARDIUM

Tuberculosis of the myocardium is apparently quite rare; only about 222 cases have been reported to date. Its actual incidence is probably greater than this, however, for microscopic involvement may easily be missed on routine necropsy examination. Three types have been observed: (1) The infiltrating type, which most frequently involves the auricles, is caused by spread of the tuberculous process from the pericardium to the myocardium. Clinically, the inception of auricular involvement may be manifested by the appearance of auricular extrasystoles, and, rarely, by auricular fibrillation.[3] Involvement of the ventricular muscle is much less common, but, nevertheless, extensive de-

struction has been observed. Caseous infiltration has been known to destroy one-half, or more, of the thickness of the ventricular wall, and may extend even to the endocardium.[4] (2) Nodular involvement of the myocardium may also occur as a part of a generalized miliary tuberculosis, but this is very infrequent. (3) Finally, there is an interstitial tuberculous myocarditis which resembles, to some extent, that caused by any fever, but is distinguished by the fact that the central infiltration, which comprises small lymphocytes, endothelial cells, a few leucocytes, and, occasionally, a Langhans cell, is much more diffuse. This type has been described by Gallavardin.[5]

### TUBERCULOSIS OF THE ENDOCARDIUM

Tuberculous endocarditis is quite rare, but a few authentic cases have thus far been reported. At Duke University, Baker[6] found endocardial tuberculosis in six of 900 consecutive necropsies on patients with pulmonary tuberculosis. In five instances, small tubercles were scattered over all parts of the endocardium as part of a generalized miliary infection. In one instance the endocardial involvement resulted from extension of a pericardial and myocardial process through the cardiac wall. White[7] reports only one case of diffuse involvement along the line of closure of a valve in which the diagnosis was probably correct. Dr. Joseph Walsh[8] states that he saw two cases of tuberculosis of the mitral valve in which the organisms were demonstrated in the tissues microscopically. The toxic action of a tuberculous process somewhere in the body does not result in sclerosis of the endocardium, or myocardial fibrosis, or calcified valvular lesions.

### EXTRACARDIAC TUBERCULOSIS

Tuberculous mediastinitis may encroach upon the branches of the pulmonary artery, causing a systolic murmur and thrill at the pulmonic area, and accentuation of the pulmonic second sound. This involvement may lead ultimately to right ventricular strain and failure.

Tuberculosis is occasionally the underlying cause of Pick's disease, or polyserositis. Although cardiac failure is rare in ordinary cases of tuberculosis, we have occasionally seen patients with tuberculous pericarditis develop enough ascites to require tapping. Pseudocirrhosis of the liver, which was associated with the pericarditis, was the underlying cause. In these cases the liver function may be good, and there is no pretibial edema.

### THE EFFECTS OF PULMONARY TUBERCULOSIS ON THE HEART

Indirectly, pulmonary tuberculosis may produce significant effects on the heart. Spontaneous pneumothorax places a sudden strain on the heart which leads to profound shock. The pulse becomes rapid, weak, and thready, and, not infrequently, death is the result. Even induced pneumothorax, which shifts the heart and mediastinal structures to one side, whether or not inflammatory lesions have partially fixed these

structures, produces a strain on the myocardium. Dyspnea, cyanosis, and tachycardia are added to the already existing symptoms until the heart becomes adjusted to the altered dynamics. The occurrence of these symptoms indicates that treatment should be conservative during the early stages of artificial pneumothorax.

Extensive chronic pulmonary involvement, which is so frequently associated with widespread pulmonary fibrosis, affects the heart unfavorably. It is quite difficult to evaluate the dyspnea, cyanosis, tachycardia, and fatigability in such cases, because most of these symptoms are common to both pulmonary tuberculosis and myocardial disease. Such extensive changes in the lungs are found to have a bad effect on the myocardium, resulting particularly in increased strain on the right side of the heart.

Paroxysmal tachycardia and paroxysmal auricular fibrillation have been known to occur in cases of tuberculosis. The cause of these disturbances in the mechanism of the heartbeat may be functional, and also obscure, just as it often is in patients who do not have pulmonary tuberculosis. If there is extensive involvement of the mediastinal lymph nodes, there is the possibility that, in some cases, encroachment on the sympathetic and vagus nerves may be an important factor in the production of these abnormalities of the cardiac mechanism. A-V nodal tachycardia is the type most frequently associated with tuberculosis.

### OTHER TYPES OF HEART DISEASE IN PULMONARY TUBERCULOSIS

The patient who has pulmonary tuberculosis, or some other form of the disease, may have had, or may develop, other kinds of heart disease. Rheumatic heart disease, particularly mitral stenosis, is observed not infrequently in association with tuberculosis. The incidence is said to be similar to that in other conditions in comparable age groups. The same is true of syphilitic aortitis and aortic insufficiency.

In cases of congenital heart disease, tuberculosis, usually of the miliary type, has often been regarded as the cause of death. The impression gained from hospital records, however, is distinctly against this. Death usually results from the congenital defect itself, or from superimposed bacterial endocarditis, and not infrequently from pneumonia.

Hypertensive heart disease is not seen frequently in association with tuberculosis. Ayman[9] found one instance among 240 cases. Fifteen per cent of all adults, and 23 per cent of those who die after the age of 50 years have hypertension.[10] A careful study of blood pressure in cases of tuberculosis, made at the White Haven Sanatorium, repeated at definite intervals, and carried on over a period of ten years, revealed that the prevalent idea that the blood pressure is generally low in cases of tuberculosis is erroneous. The blood pressure was usually at the lower limits of normal. In the advanced age groups, a high reading was often found. Only those patients who were quite ill, and had extensive

disease, had an abnormally low blood pressure, and, as they improved, there was a tendency for the blood pressure to rise. The upper and lower limits of systolic pressure which were accepted as normal were 150 and 110 to 100, respectively. Any diastolic pressure over 90 was considered abnormally high. These limits, as judged by our present-day standards, are high, and lower levels will be accepted in the near future.[11]

Coronary occlusion is seldom observed in cases of tuberculosis. Although tuberculous arteritis occurs, it has been observed but rarely in the coronary arteries,[12] and is usually confined to the smaller branches. In one reported case it did involve a comparatively large coronary branch. Three types of involvement have been observed: (1) tubercles in the intima; (2) tuberculous invasion of the adventitia, with focal or diffuse involvement of the entire wall; and (3) noncellular thickening of the intima, which, if sufficiently extensive, may lead to vascular occlusion—the so-called "contact endarteritis."

Pulmonary embolism and thrombosis often simulate coronary occlusion.[13] The manifestations include a sudden onset of precordial oppression, or actual pain, marked dyspnea or tachycardia, cyanosis or ashen pallor limited to the upper part of the body, apprehension, a rapid, feeble pulse, collapse of the peripheral circulation, a low blood pressure, and profuse perspiration. Recently, pulmonary thrombosis has been found more frequently at the White Haven Sanatorium, and, occasionally, the diagnosis is made ante mortem.

### STUDY OF PATIENTS ADMITTED TO THE WHITE HAVEN SANATORIUM

A study was made of the patients who were admitted to the White Haven Sanatorium during 1935. Those with heart disease were grouped according to age and the status of their tuberculosis. There were, in all, 418 patients, 238 men (57 per cent), and 180 women (43 per cent). Of the men, twenty-one (8.8 per cent), and, of the women, eight (4.4 per cent), were thought to have heart disease. Seventy of the patients who were admitted during 1935 died; forty-eight of these were men (68 per cent), and twenty-two were women (31.4 per cent). Thirty post-mortem examinations were performed, twenty-three on men (76 per cent), three of whom had had a diagnosis of heart disease ante mortem, and seven on women (23.3 per cent). At post-mortem examination it was discovered that ten additional patients had heart disease; seven of these were men, and three were women. Of the thirteen autopsied patients who had heart disease, seven had far-advanced pulmonary tuberculosis, four had anthracosilicosis and two were nontuberculous. Of the ten male patients, three had arteriosclerotic cardiovascular disease, three had arteriosclerosis with cardiac hypertrophy, three had cardiac hypertrophy, and one had an aortic vegetation, the etiology of which was not stated. Of the three women, two had myocardial degeneration with hypertrophy, and one had cardiac hyper-

trophy. Among the remaining seventeen post-mortem examinations, only three normal hearts were found. In the cases in which heart disease was not diagnosed during life, fourteen post-mortem examinations revealed that the pericardium was adherent, in eleven cases on both sides, in two on the right side, and in one on the left side. The myocardium was pale, flabby, and thin in eleven instances, particularly that of the right ventricle.

TABLE II

PATIENTS ADMITTED TO THE WHITE HAVEN SANATORIUM IN 1935

| | WITH HEART DISEASE | | WITHOUT HEART DISEASE | | |
|---|---|---|---|---|---|
| AGE | MALE | FEMALE | MALE | FEMALE | TOTAL |
| 7–19 years | 1 | 0 | 19 | 26 | 46 |
| 20–29 years | 4 | 4 | 58 | 86 | 152 |
| 30–39 years | 3 | 2 | 46 | 42 | 93 |
| 40–49 years | 3 | 2 | 55 | 12 | 72 |
| 50–59 years | 5 | 0 | 32 | 3 | 40 |
| 60 and over | 5 | 0 | 7 | 3 | 15 |
| Total | 21 | 8 | 217 | 172 | 418 |

CLASSIFICATION

| | WITH HEART DISEASE | | WITHOUT HEART DISEASE | | |
|---|---|---|---|---|---|
| STAGE OF DISEASE | MALE | FEMALE | MALE | FEMALE | TOTAL |
| Minimal | 1 | 2 | 20 | 17 | 40 |
| Moderately advanced | 2 | 0 | 28 | 39 | 69 |
| Far advanced | 12 | 3 | 67 | 48 | 130 |
| Nontuberculous | 6 | 3 | 34 | 13 | 56 |
| Miliary tuberculosis | 0 | 0 | 0 | 1 | 1 |
| Still in Sanatorium | 0 | 0 | 68 | 54 | 122 |
| Total | 21 | 8 | 217 | 172 | 418 |

The records of all patients with pulmonary tuberculosis who were admitted to the Philadelphia General Hospital during 1935 were analyzed. There were, in all, 1585 patients, 1017 men (64 per cent), and 568 women (36 per cent). In this series, 1000 completed records were available for study. In addition to their pulmonary tuberculosis, a clinical diagnosis of some form of cardiovascular disease was made in 8.7 per cent. These cases are summarized in Table III. It is to be noted that practically every variety of cardiovascular disease was found in association with pulmonary tuberculosis.

## SUMMARY

In pulmonary tuberculosis, the heart is normal in most instances. However, various etiologic types of heart disease may be associated with pulmonary tuberculosis. In three to five cases out of a hundred, tuberculosis may involve either the pericardium, the myocardium, or, rarely, the endocardium. The signs, symptoms, and methods of diagnosis are discussed, and their significance emphasized. Tuberculosis specialists too often overlook the presence of cardiac abnormalities because of the fact that the symptoms are similar to those caused by pulmonary disease.

TABLE III

CLASSIFICATION OF PATIENTS WITH PULMONARY TUBERCULOSIS AND CARDIOVASCULAR DISEASE ADMITTED TO THE PHILADELPHIA GENERAL HOSPITAL IN 1935

| MALES | FEMALES |
|---|---|
| *Arteriosclerotic cardiovascular disease:* | |
| 19 without complications | 7 without complications |
| 1 with auricular fibrillation and silicosis | 2 with hypertension |
| 2 with hypertension | 1 with rheumatic valvular disease |
| 1 with coronary occlusion | 1 with coronary occlusion |
| 1 with hypertension and chronic proliferative pericarditis | |
| 24 | 11 |
| Total: 35 (24 males, 11 females) | |
| *Valvular disease:* | |
| 2 mitral insufficiency (rheumatic etiology?) | 3 rheumatic mitral insufficiency |
| 1 rheumatic—double mitral and aortic | |
| 3 | 3 |
| Total: 6 (3 males, 3 females) | |
| *Hypertensive cardiovascular disease:* | |
| 5 without complications | 2 without complications |
| 1 with a positive Wassermann | 1 with arteriosclerosis |
| | 1 with mitral insufficiency and a positive Wassermann |
| | 1 with mitral insufficiency |
| 6 | 5 |
| Total: 11 (6 males, 5 females) | |
| *Luetic cardiovascular disease:* | |
| 5 without complications | |
| 1 with rheumatic endocarditis | |
| 1 with aneurism | |
| 1 with coronary occlusion | |
| 8 | |
| Total: 8 males | |
| *Pericarditis:* | |
| 1 (chronic fibrous) without complications | 1 without complications |
| 1 with hypertension and cardiac hypertrophy | 1 with rheumatic heart disease |
| 2 | 2 |
| Total: 4 (2 males, 2 females) | |
| *Endocarditis:* | |
| Total: 1 female | 1 of aortic valve |
| *Myocardial degeneration:* | |
| 5 unconfirmed | 4 unconfirmed |
| 1 confirmed by laboratory examination | 3 confirmed by autopsy |
| 1 confirmed by autopsy | 1 autopsy negative |
| 1 toxic myocarditis | 1 toxic myocarditis |
| 1 congestive heart failure (etiology?) | 1 toxic myocarditis, autopsy negative |
| 1 hypertrophy (etiology?) | 1 myocardial hypertrophy revealed by autopsy |
| 1 right ventricular hypertrophy revealed by autopsy | |
| 11 | 11 |
| Total: 22 (11 males, 11 females) | |

REFERENCES

1. Wilbur, E. Lloyd: Myocardial Tuberculosis, Am. Rev. Tubere. **38:** 769, 1938, and Custer, Edward W., and Charr, Robert: Tuberculosis of the Myocardium, J. A. M. A. **112:** 1333, 1939.
2. Beck, C. S., and Griswold, R. A.: Pericardiectomy in the Treatment of the Pick Syndrome: Experimental and Clinical Observations, Arch. Surg. **21:** 1064, 1930, and Beck, C. S., and Cushing, E. H.: Circulatory Stasis of Intrapericardial Origin: The Clinical and Surgical Aspects of Pick Syndrome, J. A. M. A. **102:** 1543, 1934.
3. Fishberg, A. M.: Auricular Fibrillation and Flutter in Metastatic Growth of Right Auricle, Am. J. M. Sc. **180:** 629, 1930.
4. Bellet, S., Gouley, B. A., and McMillan, T. M.: Nourishment of the Myocardium Through Thebesian Vessels in a Heart in Which the Large Coronary Arteries and Veins Were Destroyed by Tuberculous Myocarditis, Arch. Int. Med. **51:** 112, 1933.
5. Gallavardin, L., and Gravier, L.: Tuberculous Interstitial Myocarditis, Arch. d. mal. du coeur **21:** 472, 1928.
6. Baker, R. D.: Endocardial Tuberculosis, Arch. Path. **19:** 611, 1935.
7. White, Paul D.: Heart Disease, New York, 1931, The Macmillan Company.
8. Walsh, Joseph: Personal communication.
9. Ayman, D.: Arteriolar Essential Hypertension in Active Tuberculosis: Their Rare Association, Am. J. M. Sc. **188:** 712, 1934.
10. Adson, A. W., and Allen, E. V.: Essential Hypertension: 1. General Considerations, Proc. Staff Meetings Mayo Clinic **12:** 1, 1937.
11. Robinson, S. C., and Brucer, M.: Range of Normal Blood Pressure: A Statistical and Clinical Study of 11,383 Persons, Arch. Int. Med. **64:** 3, 1939.
12. Gouley, B. A., Bellet, S., and McMillan, T. M.: Tuberculosis of the Myocardium, Arch. Int. Med. **51:** 244, 1933.
13. Pou, Jaime F., and Charr, Robert: Thrombosis of Pulmonary Artery, Am. Rev. Tubere. **37:** 394, 1938.

# NOTE ON ELECTROCARDIOGRAPHIC NOMENCLATURE

NEUTON S. STERN, M.D.
MEMPHIS, TENN.

NAMES are short cuts of identification and should be as simple as possible. Long, descriptive phrases ought to be avoided. One such phrase, which is now accepted by virtue of its inclusion in the *Nomenclature and Criteria for Diagnosis of Diseases of the Heart*,[1] is "Elevation (or Depression) of S-T (or R-T) Segment at Origin." Others describe it as the S-T junction, or take-off.

## R-T OR S-T JUNCTION

For some time, in my own descriptions of electrocardiograms, I have used the letter J to represent junction, and have used a numeral as subscript to indicate the lead, thus: $J_3$ or $J_4$. If this idea were followed, the headings "50. Unusual Elevation of S-T (or R-T) Segment at Origin," and "51. Unusual Depression of S-T (or R-T) Segment at Origin" could be written simply "50. High (or Elevated) J," and "51. Low (or Depressed) J."

The partial description of Lead I in a case of infarction of the anterior wall of the left ventricle of a few days' duration might be $J_1$ plus, or $J_1+$, $T_1$ minus, or $T_1-$. In brief, it would be written $J_1+$, $T_1-$.

To indicate the abnormalities with greater precision, the suggestion of McGinn and White[2] may be followed, giving in tenths of a millivolt the deviation from the isoelectric level. If the take-off is elevated 0.1 mv., and T is depressed 0.3 mv., the written description would be $J_1 + 1$, $T_1 - 3$.

The R-T (or S-T) segment could be referred to simply as R-T (or S-T) or RT (or ST), with the proper subscript. It could be described as convex (curved upward), concave (curved downward), rising, or falling. Thus, $J_1 + 1$, $RT_1$ convex, $T_1 - 3$ would indicate, in Lead I, a take-off from the descending limb of R which is elevated 0.1 mv. above the isoelectric line, and is followed by a convex R-T segment which descends finally to an inverted T, 0.3 mv. below the isoelectric level.

## FOURTH LEAD NOMENCLATURE

It is now accepted usage to designate Lead I as RL, Lead II as RF, Lead III as LF. Therefore, the chest, or fourth, lead should be designated as FC instead of CF, for, by so doing, the order of the letters would indicate that the current is running in the same direction in all four leads. This would simplify the method of application of the electrodes for technicians and for beginners in electrocardiography.

Received for publication Dec. 15, 1939.

The subscript for the various positions of the chest electrodes could be appended as needed; the description of the routine fourth lead would be $FC_4$.

## SUMMARY

1. It is suggested that the origin, take-off, or junction (with R or S) of the R-T (S-T) segment be identified by the letter J (for junction), and that the lead be identified by the proper numerical subscript.

2. RT or ST would then be adequate to indicate the R-T or S-T segment. It could be further described as convex, concave, rising, or falling.

3. The designation of the customary chest lead should be FC, instead of CF, for FC indicates that the direction of the flow of current is the same as that in the standard three leads.

## REFERENCES

1. Nomenclature and Criteria for Diagnosis of Diseases of the Heart, Ed. 4, New York Heart Association, New York, Page 139, 1939.
2. McGinn, S., and White, P. D.: The Duration of the QRS Complex in the Normal and in the Abnormal Electrocardiogram, Am. Heart J. 9: 642, 1934.

899 Madison Avenue

# Department of Clinical Reports

## COARCTATION OF THE AORTA IN A CHILD WITH ARRESTED SUBACUTE BACTERIAL ENDARTERITIS AND A CALCIFIED MYCOTIC ANEURYSM AT THE SEAT OF STRICTURE*

GERTRUDE H. B. NICOLSON, M.D.
NEW YORK, N. Y.

THIS is the report of an unusual case of coarctation of the aorta, in a child, complicated by subacute bacterial endocarditis and endarteritis, with the development of a mycotic aneurysm of the descending thoracic aorta at the point of constriction. Furthermore, calcification has been developing in the walls of the sac, and the child appears to have recovered from the active, infective process.

Coarctation of the aorta of the adult type may be defined as a congenital stenosis, or a complete atresia, of the descending arch at, or near, the insertion of the ductus arteriosus. It is explained, at least in many of the cases, as the result of an abnormal extension into the contiguous wall of the aorta of the obliterative process which normally takes place in the ductus in the first weeks of postnatal life. In others, it would seem to be a true arrest of development of the fourth, left, aortic arch.

The degree of the stenosis is balanced by the amount of collateral circulation which develops between the branches given off above, and those below, the constriction. Usually, all of the vessels to the head and upper extremities arise proximal to the coarctation, which produces a relative increase of the blood supply to these parts, as evidenced by marked, bounding pulsation, a ruddier color of the face, and a higher level of intelligence than the subject might otherwise have had.

The condition is not common. It occurred as a primary lesion in 7 per cent of the thousand cases of congenital heart disease analyzed by Abbott.[1] The diagnosis is based on the combination of elevated blood pressure in the upper extremities with an absent, or diminished, pressure in the lower, abnormal pulsation of the enlarged collateral vessels above, with absent femoral pulsations, and, in the roentgenogram, "scalloping" of the ribs and, frequently, absence of the aortic knob.

Since the appearance, in 1928, of Abbott's[2] classic analysis of 200 collected cases of coarctation with autopsy, this condition has become familiar to all, and no attempt will be made here to discuss in detail the clinical features or to review the literature. It is to be noted, how-

*Read before the Section of Medicine, New York Academy of Medicine, April 18, 1939. From the Department of Pediatrics, Columbia University and St. Luke's Hospital, Service of Dr. F. Elmer Johnson.
Received for publication Oct. 16, 1939.

ever, that, of these 200 cases, death was caused in fourteen (7 per cent) by an infective endarteritis, with the resultant formation of a mycotic aneurysm. The process is identical with the almost constantly fatal invasion of the heart in subacute bacterial endocarditis, in which the prominent feature is an intrusion of the infective agent, commonly the *Streptococcus viridans*, into the tissues of an already diseased or congenitally malformed valve. In this connection, it is to be noted that the aortic valve is bicuspid in a relatively large proportion of cases of coaretation (nearly 25 per cent in Abbott's 200 collected cases), and this provides a favorable nidus for the infective process. Congenital subaortic stenosis, caused by an annular, fibrous shelf lying a short distance below the valve, also may occur with coaretation, and may be the seat of bacterial invasion.

In this connection, it is interesting to recall the recent work of Kinsella and Muether,[3] who produced experimental bacterial endocarditis in dogs, both by intravenous and oral administration of *Streptococcus viridans*. Dogs with previously traumatized heart valves developed bacterial endocarditis and ran a typical clinical course, with a fatal outcome. Dogs with normal valves escaped infection. One must bear in mind that the valves in the dogs with bacterial endocarditis were damaged by trauma and not by disease. Perhaps this is the reason why sulfanilamide and merthiolate were highly successful in the treatment. It would be interesting to see what the effect of this treatment would be on reinfected, cured dogs whose valves would therefore have been damaged by disease.

Richey,[4] in a study of 41 collected cases of aneurysm of the thoracic aorta in persons under 18 years of age, found a mycotic lesion in 20, and four of the latter also had coaretation of the aorta. Because of the kinking and wrinkling of the aorta in the area immediately distal to the stricture, and the eddying of currents here, this point is commonly the site of the mycotic aneurysm. Thus, in 13 of the 14 instances of this condition which were cited above,[2] the aneurysm was at or below the seat of constriction. Rupture occurred in three of these. In one case, that of a girl of 12 years, the aneurysmal site was just distal to the constriction, and rupture took place into the left bronchus.[5] In another case, a boy, aged 10 years, had a mycotic aneurysm distal to the coaretation which ruptured into the esophagus.[6] In the third, a lad of 17 had a mycotic aneurysm 1 cm. below the constriction which ruptured into the left pleural cavity.[7]

The course in subacute bacterial endocarditis or endarteritis is long-drawn-out, and similar in many respects to any chronic infection. Rarely have recoveries from this usually fatal disease been reported. Libman says that "subacute bacterial endocarditis is a disease in which healing can occur from the bacterial, pathological, and clinical standpoints." He has witnessed seventeen spontaneous recoveries.[8] In the

present state of our knowledge, however, therapeutics offers little hope of cure. The various forms of treatment that have been tried have almost invariably proved to be unsuccessful. The newer chemotherapeutic agents may offer more hope in the future.

The case now to be presented illustrates several of the above-mentioned features.

## CASE REPORT

The patient, a girl of 12 years, first visited the Children's Medical Clinic of St. Luke's Hospital in May, 1931, when she was 5 years old. She was suffering from acute tonsillitis, headache, and fever. She was fair, tall, and thin. She weighed 8½ pounds at birth; the delivery was normal. She was the third child of apparently healthy, young, Irish parents. She had had pneumonia at the age of 5 weeks, and diphtheria when she was one year old.

On physical examination, a systolic murmur, which was loudest over the right side of the base of the heart, was heard. It was then regarded as a congenital heart murmur of little clinical significance. No thrill, clubbing of the fingers, cyanosis, or dyspnea was noted. The child lived on the fifth floor and had run up and down stairs many times daily without difficulty.

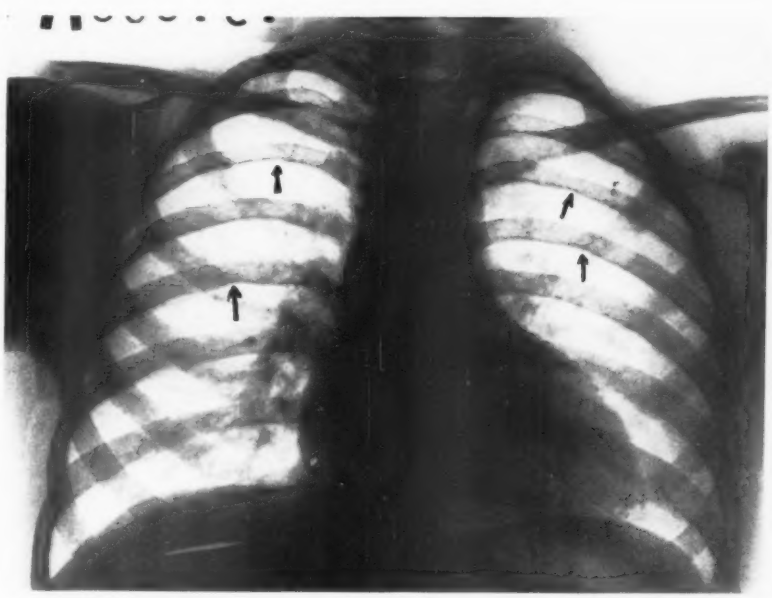


Fig. 1.—Teleoroentgenogram taken July 6, 1936, at onset of infection. Note absence of aortic knob and early notching of ribs (black arrows).

She had her tonsils removed in May, 1933, after frequent attacks of tonsillitis. She kept returning to the children's medical clinic, and it was noted that the character of the systolic murmur at the base of the heart varied somewhat; it was usually soft and low in pitch. A diagnosis of coarctation of the aorta was made when it was discovered that the blood pressure was 180/90 in the upper extremities, and 110/90 in the popliteal arteries. (Following rest, the blood pressure dropped to 140/90 in the brachial arteries and could not be measured in the popliteal arteries.) Forceful brachial pulsations were present, but there were no femoral pulses. Intercostal arterial pulsations were palpable. The retinal

vessels were tortuous and pulsating. Slight notching of the ribs and absence of the aortic knob were noted in the teleoroentgenogram (Fig. 1). Polygraphic tracings of the radial and femoral pulses showed that the femoral pulse was smaller and had a slow rise and fall (Fig. 2).

On July 3, 1936, the child, then 10 years old, came to the clinic complaining of precordial pain, fever, and headache. A loud, rumbling, systolic murmur of a different character was heard over the aortic area and the back, and the spleen was palpable. The child was admitted to the ward for observation because it was thought that she might have subacute bacterial endocarditis engrafted upon a subaortic stenosis or congenitally bicusped aortic valve.

On admission, the temperature ranged between normal and 103° F. The hemoglobin was 50 per cent. The erythrocyte sedimentation rate was 80. The leucocytes numbered 16,000, of which 78 per cent were polymorphonuclears. Two weeks after admission, a tender, red spot appeared on the plantar surface of the terminal phalanx of the left toe, became purple, and disappeared in a few days. This was the first of many embolic phenomena which occurred during the period between July, 1936, and February, 1937. Petechiae also appeared frequently, mostly on the lower extremities. The child was pale, and a secondary anemia, with a hemoglobin of 50 to 60 per cent, continued for several months. Serial electrocardiograms showed that left axis deviation, which had not been present in 1931, was developing.

On July 23, twenty days after admission, the blood culture was positive for *Streptococcus viridans*. The culture was again positive for the same organism on August 6.

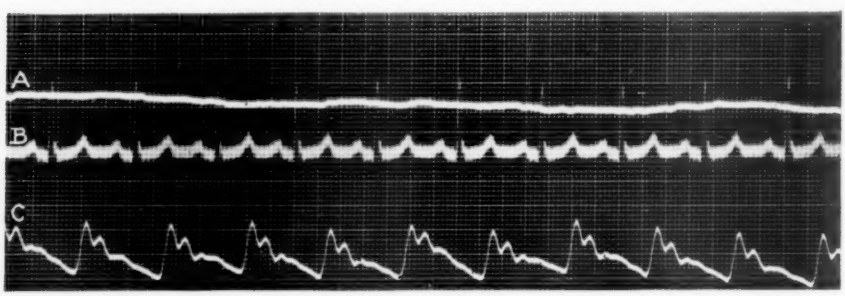



Fig. 2.—Polygraphic tracings taken simultaneously with electrocardiogram. *A*, Femoral curve is extremely low, and the start of the wave is slightly later than that of the radial. *B*, Lead I of electrocardiogram, showing no abnormality. *C*, Radial pulse tracing.

On July 24, severe pain occurred in the left upper quadrant of the abdomen, and the spleen became extremely tender. This was thought to be caused by splenic infarction. This complication recurred on August 13 and October 8. On November 7 there was severe pain in the left kidney region, followed by hematuria. These symptoms were indicative of infarction of the left kidney.

A teleoroentgenogram which was made September 5, two months after admission, showed a new shadow in the area of the pulmonary artery. In the left anterior oblique view this was seen to be in the position of the descending portion of the arch of the aorta. The barium-filled esophagus was displaced to the right.

During this time the child was treated symptomatically. She was given five blood transfusions, of 250 c.c. each, by the direct method. Codeine and other sedatives were used to relieve pain. She was put on a high-caloric, high-vitamin diet, and received ultraviolet irradiation at regular intervals throughout her illness.

Toward the end of December, 1936, a change was noted in the temperature curve. The high peaks no longer occurred. On February 5 the temperature was

normal, and the child became symptom-free. During the spring and summer of 1937, she was carefully watched for signs of latent subacute bacterial endocarditis. However, she has had no recurrence of fever or other symptoms from that time to date, an interval of two years. At the present time the child appears well and happy. She has a home teacher, with whom she is progressing rapidly. She has gained satisfactorily in weight and in height, and has no symptoms referable to her heart disease.

The teleoroentgenogram which was made in January, 1939 (Fig. 3), showed fine white lines of calcification around the periphery of the aneurysm. (These began to appear in the roentgenogram sixteen months after admission.) The left ventricle was enlarged, and the size of the aneurysmal shadow had increased slightly. The "scalloping" of the ribs was more marked than on earlier examinations.

## SUMMARY

A case of subacute bacterial endocarditis and endarteritis, with apparent recovery, is reported in a child who has coaretation of the aorta of the adult type, and now, as a result of the endarteritis, has a mycotic aneurysm, with calcification of its walls, which is situated in the descending arch, apparently at the seat of the coaretation.

## ADDENDUM

Since the above observations were made, the chambers of the patient's heart and her great vessels have been visualized by a radiopaque substance, diodrast. This procedure[9] was carried out by Dr. George P. Robb and Dr. Israel Steinberg, to whose courtesy I am indebted for the following illustrations: Figs. 4, 5, 6, 7*A* and 7*B*. (The overlay tracing and the legends were made by Dr. Ursula Roche and Dr. Stewart F. Alexander.)

The operation was simple and unaccompanied by any untoward reaction. There was a preliminary fluoroscopic examination to find preferred angles of the heart, and also an accurate measurement of the circulation time (to ascertain the time required to fill the right and left sides of the heart). The child was then held in place before the screen by wide straps, and diodrast was rapidly injected into the raised arm through the median basilic vein. Films were taken in rapid succession at predetermined intervals. The patient complained of a sensation of heat during the injection, and had some allergic reaction, as evidenced by swelling of the lips. However, the symptoms must not have been very serious, for half an hour later the child ate a very substantial lunch.

I should like to draw special attention to the work of these investigators. I feel that this method opens a new chapter in the study of congenital heart disease. Anatomic abnormalities of the heart or great vessels, when accurately visualized in this way, may become amenable to surgical correction. In the case presented herewith, the possibility of wiring, ligating, or even removing the aneurysm suggests itself, since it might prevent rupture of the aneurysm and sudden death.

Fig. 3.

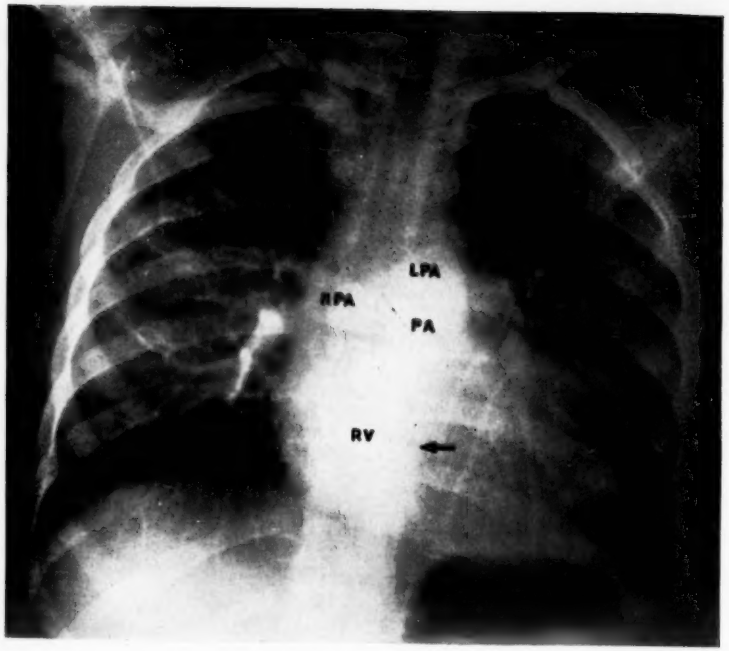



Fig. 4.

Fig. 3.—January, 1939. Posteroanterior view, showing enlarged left ventricle, above which extends the convex shadow of the aneurysm. Note areas of calcification in the periphery of the aneurysm. Compare with contrast films, Figs. 4 and 5.

Fig. 4.—Contrast roentgenogram. Posteroanterior view taken 3 seconds after beginning of injection of opaque substance. The right-sided chambers of the heart are outlined. The right axillary, subclavian, and innominate veins, the superior vena cava, the right ventricle, and the pulmonic artery, with its right and left branches and arborizations within the lungs, are clearly seen. Black arrow indicates interventricular septum. Note that the aneurysmal shadow is not filled, and lies outside the pulmonary artery.

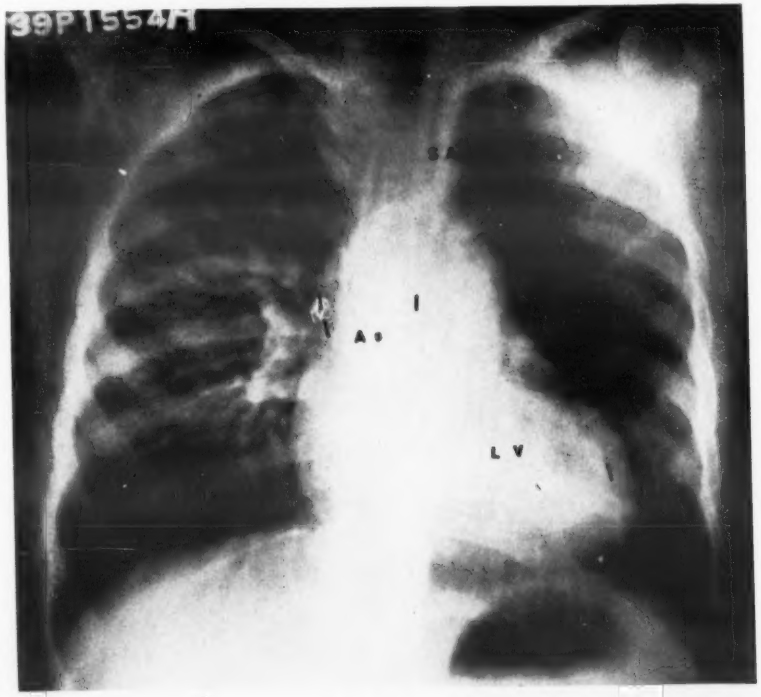



Fig. 5.

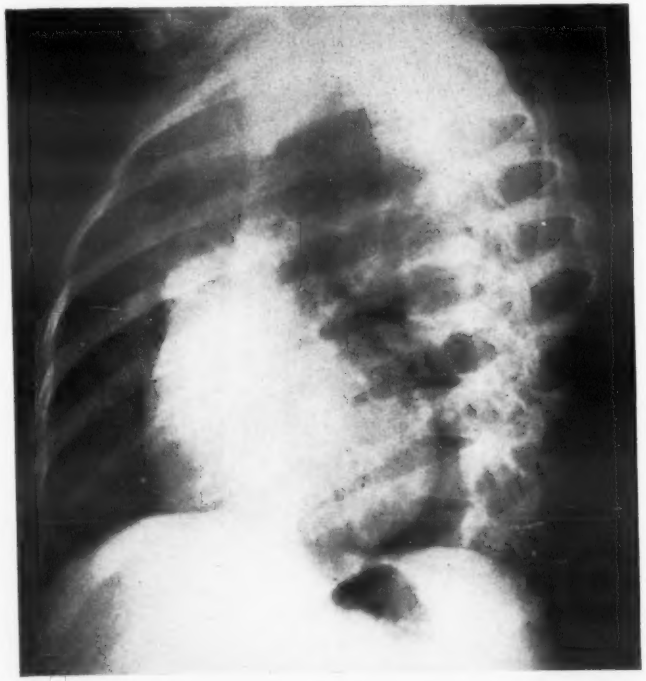


Fig. 6.

Fig. 5.—Contrast roentgenogram. Posteroanterior view taken 8 seconds after injection, showing filling of the left side of the heart. The left ventricle and descending aorta and the aneurysm are filled with contrast medium. Note the thickness of the left ventricular wall, the dilated left subclavian artery, and the collateral arterial circulation over scapulae.

Fig. 6.—Conventional roentgenogram. Left anterior oblique position. Note poor definition of supracardiac vascular structures, enlargement of left ventricle, and aneurysmal shadow posterior to bifurcation of the trachea. The left bronchus appears to be displaced anteriorly and downward by the aneurysm. Note the shadow of the ligamentum arteriosum, which is seen, in this and the succeeding illustrations, as a band extending from the pulmonic artery to the aneurysm. It does not fill with contrast medium, and is constantly present in this case.

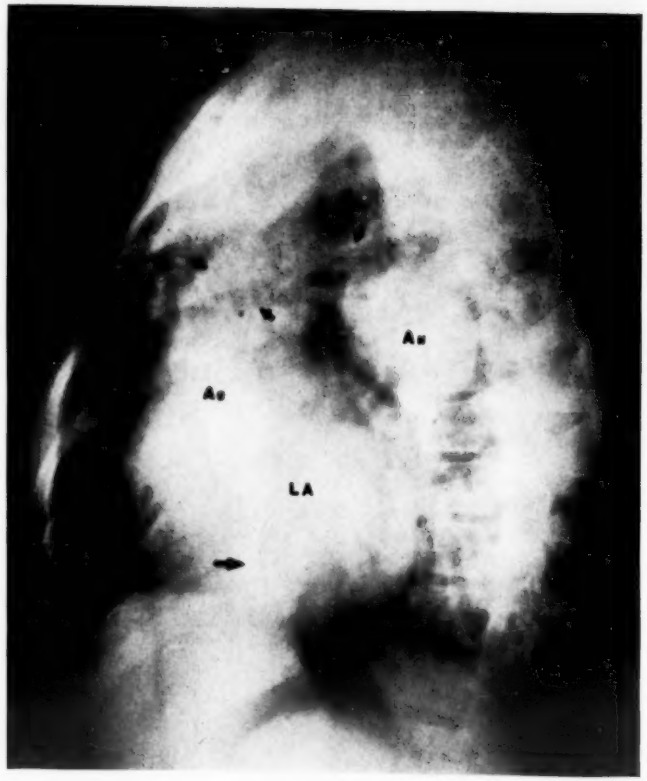



Fig. 7A.

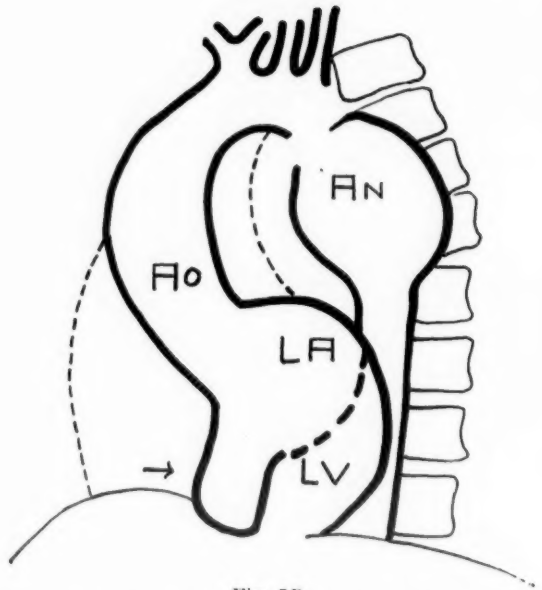



Fig. 7B.

Fig. 7A.—Contrast roentgenogram. Left anterior oblique view, 8 seconds following the injection. The left auricle, the left ventricle, and the aorta are visualized. The left ventricle is indistinct, as if in early diastole. Lowest black arrow denotes the interventricular septum and, probably, stream of blood entering left ventricle from left auricle. The intercardiac origin of the aorta is clearly seen. The ascending aorta is dilated, but the arch shows progressive narrowing to a point just beyond the origin of the left subclavian artery, where the maximal constriction is noted (upper left arrow). Immediately below this, the aneurysm is clearly outlined, and the contrast medium is seen entering the descending aorta.

Fig. 7B.—*LA*, left auricle; *LV*, left ventricle; *Ao*, aorta; *An*, aneurysm. Note branches to neck from arch of aorta. Arrow indicates interventricular septum and stream of blood flowing into left ventricle.

Surgical intervention, however, in a child whose present condition appears to be excellent is certainly to be approached with caution.

I wish to thank Dr. Maude E. Abbott and Dr. F. Elmer Johnson for valuable suggestions.

REFERENCES

1. Abbott, M. E.: Atlas of Congenital Cardiac Disease, New York, 1936, American Heart Association.
2. Abbott, M. E.: Coaretation of the Aorta of the Adult Type, Am. Heart. J. 3: 381, 1928.
3. Kinsella, R. A., and Muether, R. O.: Experimental Streptococcic Endocarditis, Arch. Int. Med. 62: 246, 1938.
4. Richey, DeWayne G.: Intrapericardial Rupture of Aortic Aneurysm in a Boy Sixteen Years of Age, Arch. Int. Med. 31: 232, 1923.
5. Libman, E.: Report by M. E. Abbott in Blumer's Bedside Diagnosis 2: 376, 1928.
6. Reifenstein, B. W.: Two Cases of Mycotic Aneurysm, Am. J. M. Sc. 168: 381, Case 2, 1924.
7. Smith, F. M., and Hansmann, G. H.: Mycotic Aneurysm of Aorta, Arch. Int. Med. 38: 367, 1926.
8. Libman, E.: Study of Endocardial Lesions of Subacute Bacterial Endocarditis With Particular Reference to Healing or Healed Lesions, Am. J. M. Sc. 144: 313, 1912.
9. Robb, George P., and Steinberg, Israel: A Practical Method of Visualization of Chambers of the Heart, the Pulmonary Circulation, and the Great Blood Vessels in Man, J. Clin. Investigation 17: 507, 1938.

# ORTHOSTATIC PAROXYSMAL AURICULAR TACHYCARDIA WITH UNUSUAL RESPONSE TO CHANGE OF POSTURE

## Report of a Case

M. James Fine, M.D., and Ralph Miller, M.D.
Newark, N. J.

AN ATTACK of paroxysmal auricular tachycardia may occasionally be precipitated or terminated by certain changes of posture. The heart rate when a paroxysm is in progress, however, is affected inappreciably, if at all, by change of posture.[1] So rigid is this rule that an exception may be regarded as a curiosity.

We are prompted to report the following case because it is remarkable in two respects. Over a period of two years, unless it was prevented by digitalis or quinidine therapy, paroxysmal auricular tachycardia occurred invariably when the patient assumed the sitting or standing position. Of perhaps greater interest was the marked response of the rate of the tachycardia to change of position.

### CASE REPORT

O. H., a 16-year-old white schoolgirl, was referred to the Cardiac Clinic of the Newark City Health Department in October, 1937, because of tachycardia. Since 1931 she had experienced recurrent attacks of pain and swelling of the joints of undetermined etiology. The knee, elbow, and wrist joints were involved symmetrically. In July, 1935, she was found to have prenatal syphilis, and appropriate therapy was instituted.

The chief complaint was abnormal fatigability. There were but slight dyspnea and palpitation on unusual exertion or excitement. For several years she had noticed weakness, dizziness, and, occasionally, syncope, upon standing erect. These symptoms were particularly annoying when she arose from bed after a sleep. Headaches occurred very frequently. She practically never perspired, and was greatly distressed by hot weather. The menses were scant and irregular, and there was moderately severe dysmenorrhea.

Her father was suffering from syphilis and pernicious anemia. Her mother and sister also had syphilis. A brother had died of acute appendicitis.

*Physical Examination.*—The patient was a fairly well-developed adolescent girl of average intelligence. She weighed 104 pounds and was 4 feet 10.5 inches tall. There was no abnormal pigmentation of the skin or mucous membranes.

The pupils were irregular, unequal, slightly dilated, and reacted sluggishly to light. The upper central incisors were typical Hutchinson's teeth. The tonsils were not obviously diseased. The thyroid gland was not enlarged. The thoracic contour and the lungs were normal. The apex beat was within normal limits. No thrills or abnormal pulsations were present. The heart rate (seated) was 180 per minute, and the beating was regular. The heart sounds were normal at the apex, but the pulmonic second sound was split. No murmurs were audible. The blood pressure was 80 (?) mm., systolic, and 60, diastolic.

From the Cardiac Clinic, Newark Health Department, Newark, N. J.
Received for publication Nov. 7, 1939.

No abdominal organs or masses were palpable. The kneejerks were hyperactive.

*Laboratory Data.*—The erythrocytes numbered 4,710,000, and the hemoglobin was 90 per cent. The leucocyte count was 9,500, and the differential count showed 74 per cent polymorphonuclear leucocytes, 22 per cent lymphocytes, 2 per cent eosinophiles, 1 per cent basophiles, and 1 per cent monocytes. The urine was normal. The blood sugar level was 80 mg. per 100 c.c., and the blood urea, 14 mg. per 100 c.c.

The blood Wassermann reaction was strongly positive (4 plus). Examination of the spinal fluid gave the following results: Wassermann reaction, anticomplementary; globulin, positive; cell count, 7; colloidal gold curve, 5555320000.

On three occasions the basal metabolic rate was −25 per cent, −26 per cent, and −13 per cent, respectively. The Mantoux tuberculin reaction was negative with 0.1 c.c. of 1:100 O. T. The vital capacity was normal (2,900 c.c.).

A teleroentgenogram showed a hypoplastic type of heart. Roentgenograms of the knee joints showed nothing abnormal.

Electrocardiograms which were taken shortly after admission showed a heart rate of 150 per minute. The auricular complexes were indistinguishable because they were fused with the T waves. At this time, these tracings were thought to show sinus tachycardia.

*Additional Cardiovascular Studies.*—During the past two years the patient has reported for examination more than sixty times. When she was not taking an adequate amount of digitalis or quinidine, she invariably had a marked tachycardia, which was of particular interest because of its response to change of posture. For example, the pulse rate was usually about 120 per minute in the recumbent position, 150 in the sitting and 180 in the standing. The range in pulse rate in the recumbent position was from 80 to 140, in the sitting, from 108 to 180, and in the standing, from 136 to 200 per minute. The difference between the recumbent and standing rates was never less than 40 beats per minute, and the rate in the sitting position was usually about the mean of the other two.

The heartbeat was always regular when she was in the erect posture. Rarely, dropped beats were noted when she was in the sitting position. The heartbeat was most often irregular during recumbency. Elevation of the foot of the bed accentuated the irregularity and retarded the pulse rate.

The change in pulse rate when the patient passed from the horizontal to the vertical position was instantaneous. When she changed from the vertical to the horizontal, however, the alteration in rate was sometimes abrupt, and sometimes gradual.

The pulse rate was accelerated by exercise only on the rare occasions when the rate in the erect posture was below 150 per minute. When the patient was standing, the application of oculobulbar or carotid sinus pressure did not retard the pulse rate or restore normal rhythm. There was no response to the Valsalva experiment.

It was possible, by administering digitalis or quinidine, to maintain the pulse rate at a normal level, i. e., about 90 per minute in the supine, and 96 in the standing, position.

The blood pressure was usually between 90 and 100 mm. Hg, systolic, and 60 and 75, diastolic. Its postural variations, however, were within normal limits (Table I). The blood pressure was not significantly altered by digitalis or quinidine. The application of a tight abdominal binder did not influence the blood pressure or pulse rate.

*Analysis or Electrocardiograms.*—Electrocardiograms which were taken in the erect posture on five occasions showed paroxysmal auricular tachycardia. On June 29, 1939, the rate was 162 per minute and practically constant (Fig. 1). The P wave was inverted in Lead I and upright in Leads II and III. The ectopic focus was therefore thought to be located in the left auricle.[2] The P-R interval

was normal. There was electrical alternation of the QRS complexes in all leads, and of the T wave in Lead IVF.

In the sitting position the heterotopic rhythm persisted, although at a considerably slower rate (Fig. 2). Minor differences in the contour of the P waves, as compared to those in Fig. 1, were noted, but were ascribed to the postural change rather than to a shift of the pacemaker. The rate was not constant; it varied from 130 to 144 per minute. On other occasions, when the rate in the sitting position was more rapid, minor degrees of electrical alternation were observed.

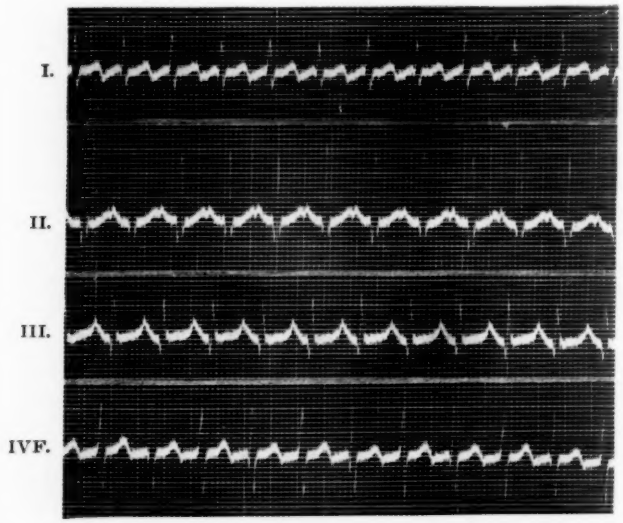



Fig. 1.—Electrocardiograms taken June 29, 1939, with the patient standing. Paroxysmal auricular tachycardia; rate, 162 per minute. P wave inverted in Leads I and IVF. Electrical alternation of $Q_1$, $R_1$, $S_1$, $Q_2$, $R_2$, $Q_3$, $Q_4$, $R_4$, $S_4$, and $T_4$.

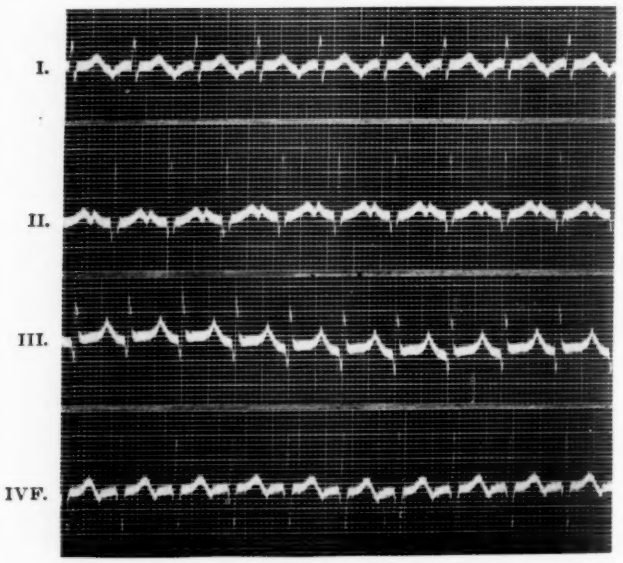



Fig. 2.—Electrocardiograms taken immediately after those in Fig. 1, with the patient sitting. Rate reduced and inconstant, varying from 130 to 144 per minute.

TABLE I

SELECTED RECORDS OF PULSE RATE AND BLOOD PRESSURE IN SUPINE, SITTING, AND STANDING POSITIONS

| DATE | PULSE | | | BLOOD PRESSURE | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | SUPINE | | SITTING | | STANDING | |
| | SUPINE | SITTING | STANDING | SYSTOLIC | DIASTOLIC | SYSTOLIC | DIASTOLIC | SYSTOLIC | DIASTOLIC |
| 7/ 7/38 | 100 | 128 | 160 | 98 | 70 | 96 | 70 | 90 | 75 |
| 7/ 8/38 | 120 | 180 | 180 | 95 | 60 | 90 | 70 | 90 | 70 |
| 7/14/38 | 120 | 150 | 180 | 105 | 60 | 98 | 70 | 90 | 75 |
| 9/27/38 | 140 | 160 | 200 | | | | | | |
| 2/14/39 | 80 | 136 | 136 | | | | | | |
| 4/27/39 | 80 | 108 | 150 | 96 | 60 | 95 | 64 | 88 | 65 |
| 5/11/39 | 138 | 150 | 180 | 96 | 68 | 88 | 70 | 86 | 70 |
| 6/20/39 | 88 | 140 | 160 | 100 | 60 | 96 | 60 | 94 | 70 |
| 8/23/39 | 80 | 150 | 186 | | | | | | |

When the patient was recumbent, the following variations in the behavior of the rate and rhythm occurred at different times:

1. Normal sinus rhythm was restored (Fig. 3).

2. The auricular tachycardia persisted, but at a slower rate than in the sitting or standing position. Thus, on July 13, 1938, the rate when she was standing was 188 per minute, when she was sitting, 150, and, when she was recumbent (Fig. 4), it was between 120 and 125.

Fig. 3.—Electrocardiograms taken immediately after those in Fig. 2, with the patient supine. Normal sinus rhythm; rate about 90 per minute.

3. There were repeated, short runs of paroxysmal auricular tachycardia, interrupted by isolated beats of sinoauricular origin. During the runs of tachycardia, incomplete auriculoventricular block, with Wenckebach's phenomenon, occurred. The auricular complexes appeared to be polymorphic. We believed that this was caused by differences in points of incidence of the P waves upon the preceding T waves,

rather than by an actual shift of the pacemaker. The T waves showed interesting variations in amplitude (Fig. 5).

## COMMENT

As far as we have been able to ascertain, this case, in which paroxysmal auricular tachycardia invariably occurred when the upright position was assumed, is unique. The only comparable case in the literature is that of Sanders,[3] in which orthostatic tachycardia accompanied orthostatic hypotension. The pulse rate doubled abruptly when the patient changed from the supine to the standing position, and this increase was approximately halved when he assumed the sitting position. Pulse irregularities were observed at times, but their character was not ascertained. However, Sanders did not definitely classify the tachycardia, and his electrocardiographic studies were not complete.

Since the exact mechanism of the production of paroxysmal auricular tachycardia remains unknown, any attempt to explain its constant occurrence as an orthostatic phenomenon is necessarily a matter of sheer speculation. Local changes in excitability caused by inadequate blood supply to the myocardium may be a factor of importance. In this connection, Akesson[4] demonstrated in instances of orthostatic arterial ischemia that the T wave was negative and the S-T segment depressed; these changes are regarded as a result of myocardial anoxemia. More logically, perhaps, the explanation is to be found in changes in the activity of the extrinsic cardiac nerves.

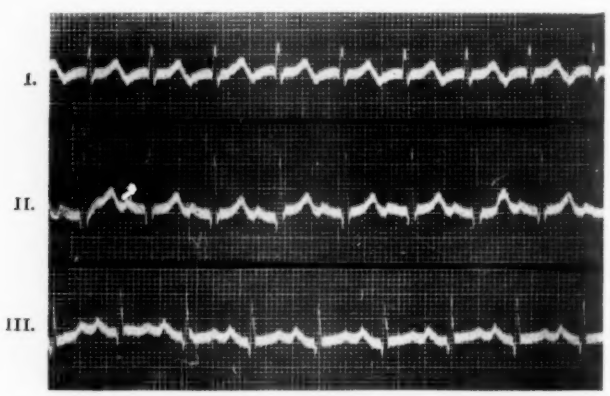



Fig. 4.—July 13, 1938. Supine position. Paroxysmal auricular tachycardia; rate, 120 to 125 per minute.

It is generally accepted that assumption of the supine position increases the vagal tone. This is caused by the increased flow of blood to the head, which results in stimulation of the vagal centers, either directly or reflexly, by way of the carotid sinus. In the upright position, on the contrary, there is a tendency toward massing of blood in the splanchnic area and lower extremities, and, consequently, vagal activity is indirectly lessened.[5]

There is considerable evidence that the onset of paroxysmal auricular tachycardia may coincide with sudden diminution in vagal tone. The attacks which follow fright, anger, excitement, and other emotions are probably to be attributed to this factor. Galli[6] succeeded in precipitating paroxysmal auricular tachycardia in a patient by the administration of atropine. Otto and Gold[7] had a similar experience with epinephrine. Graber[8] observed an interesting case of Hodgkin's disease in which frequent attacks of paroxysmal auricular tachycardia occurred. At autopsy, the vagi were found to be degenerated as a result of pressure by enlarged mediastinal lymph nodes.

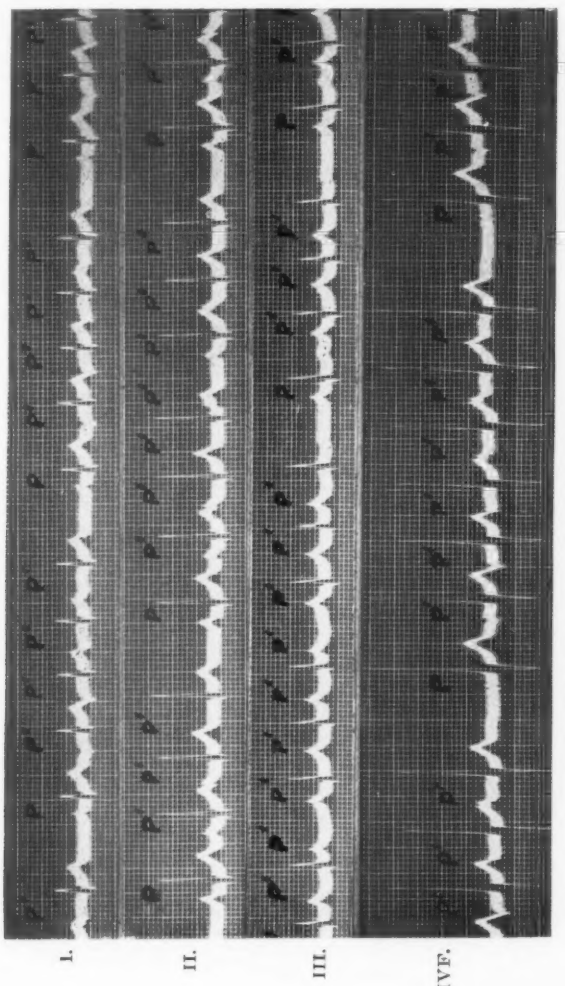



Fig. 5.—Oct. 13, 1938. Patient supine. Normal auricular complexes designated *P*; ectopic complexes, *P'*. Short runs of paroxysmal auricular tachycardia, during which there are incomplete A-V block, with Wenckebach's phenomenon, and variations in the amplitude of the T waves.

It may be assumed that, in our case, a potential ectopic focus becomes activated in the erect posture as a result of diminished vagal activity. We do not believe that the theory of parasystole[9] is applicable, for

reference to Fig. 5 will demonstrate that the longer intervals between ectopic P waves are not exact or approximate multiples of the shortest P′-P′ intervals.

Theoretically, the nonspecialized auricular tissue is under only partial nervous control. Although the onset or termination of an attack of paroxysmal tachycardia may be related to changes in the activity of the vagus, the heart rate in a given paroxysm remains remarkably constant, and does not respond to stimuli which influence the normal sinus rhythm. Rarely, there are exceptions to the rule. Iliescu and Sebastiani[10] reported a case in which conspicuous slowing of the rate occurred during quinidine therapy. Maddox[11] described a case of paroxysmal tachycardia (possibly nomotopic) of exceptional duration and gradual decline, in which the heart rate responded to some extent to rest, exercise, emotions, and sleep. In our case, the heart rate during the tachycardia varied with posture and rarely with exercise.

It is possible that, in these exceptional cases, there is either a difference in the nerve distribution to the auricle, or an anomaly of the tissue comprising the ectopic focus, so that it possesses properties approaching those of the sinus node itself. Rothberger and Sachs[12] believe that islets of sinoauricular tissue might occur in the left auricle, which would account for some instances in which this structure exhibited automatism. Indeed, Segre[13] claimed to have traced sinoauricular nodal tissue into the left auricle.

The fact that the tachycardia rate is slower in the sitting position than in the standing position is probably the result of reflex stimulation of the vagus by afferent impulses from the lower extremities.[5] Further diminution of the rate, or termination of the paroxysm when the patient lies down, may be caused by stimulation of the carotid sinus or vagal centers by the increased flow of blood to the head.

The presence of incomplete A-V block during runs of tachycardia in the recumbent position is also to be considered as a manifestation of enhanced vagal tone. Alexander and Bauerlein[14] and Santucci[15] described cases of clinostatic heart block which they attributed to vagal influences.

Electrical alternation is an indication that the heart is overtaxed. In paroxysmal auricular tachycardia this may be caused by shortening of the diastolic rest period.[16] The occurrence of electrical alternation in our case in the erect posture, and in the sitting position only when the pulse rate was very rapid, is to be explained in this way.

## SUMMARY

A bizarre case is reported, in which paroxysmal auricular tachycardia invariably occurred in the sitting or standing positions, unless held in abeyance by digitalis or quinidine therapy.

The rate of the tachycardia changed with change of position. The rate was slower in the sitting than in the standing position, and, unless normal sinus rhythm were restored, it was further reduced by recumbency. The heart rate was accelerated, on rare occasions, by exercise, but did not exhibit other sinus reactions.

Frequently, there were short runs of paroxysmal auricular tachycardia in the recumbent position, during which incomplete A-V block, with Wenckebach's phenomenon, occurred.

Electrical alternation was noted during the tachycardia in the erect position, and to a lesser degree in the sitting position when the rate was sufficiently rapid.

We are deeply indebted to the numerous cardiologists who reviewed this case with us and helped us to reach a solution of a most intricate problem.

## REFERENCES

1. Lewis, T.: Mechanism and Graphic Registration of the Heart-beat, London, 1920, Shaw and Sons, p. 244.
2. Abramson, D. I., Fenichel, N. M., and Shookhoff, C.: Study of Electrical Activity in Auricles, AM. HEART J. **15**: 471, 1938.
3. Sanders, A. O.: Postural Hypotension with Tachycardia; A Case Report, AM. HEART J. **7**: 808, 1932.
4. Akesson, S.: Electrocardiographic Changes in Presence of Orthostatic Circulatory Disturbances, Year Book of General Medicine, Chicago, 1938, Year Book Publishers, p. 623.
5. MacWilliam, J. A.: Postural Effects on Heart-rate and Blood Pressure, Quart. J. Exper. Physiol. **23**: 1, 1933.
6. Galli, G.: Attacks of Paroxysmal Auricular Tachycardia Following Atropine, Heart **7**: 111, 1918-1920.
7. Otto, H. L., and Gold, H.: Auricular Paroxysmal Tachycardia; The Effects of Epinephrine, Quinine, Quinidine, Atropine and Digitalis, AM. HEART J. **2**: 1, 1926.
8. Graber, V. C.: Paroxysms of Tachycardia in Case of Hodgkin's Disease in Which Vagus Nerves Were Degenerated by Pressure of Enlarged Mediastinal Glands, AM. HEART J. **1**: 564, 1926.
9. Kaufmann, R., and Rothberger, C. J.: Beiträge zur Enstehungsweise extrasystolischer Allorhythmien, Ztschr. f. d. ges. exper. Med. **7**: 199, 1918-1919.
10. Iliescu, C. C., and Sebastiani, A.: Notes on the Effects of Quinidine Upon Paroxysms of Tachycardia, Heart **10**: 223, 1923.
11. Maddox, K.: Auricular Paroxysmal Tachycardia (Possibly Nomotopic) with Variable Auriculo-Ventricular Conduction Time; Case of Exceptional Duration, With Gradual Slowing of Rate, AM. HEART J. **14**: 183, 1937.
12. Rothberger, C. J., and Sachs, A.: Rhythmicity and Automatism in the Mammalian Left Auricle, Quart. J. Exper. Physiol. **29**: 69, 1939.
13. Segre, R.: Quoted by Rothberger and Sachs.[12]
14. Alexander, H. L., and Bauerlein, T. C.: Influence of Posture on Partial Heart-Block, AM. HEART J. **11**: 223, 1936.
15. Santucci, G.: Su due casi di blocco cardiaco parziale clinostatico, Cuore e circolaz. **16**: 441, 1932.
16. Fishberg, A. M.: Heart Failure, Philadelphia, 1937, Lea & Febiger, p. 81.

# Department of Reviews and Abstracts

## Selected Abstracts

**Piccione, Frank V., and Scherf, David: The Rhythmic Formation of Coupled Beats and Paroxysmal Tachycardias in the Outer Layers of the Myocardium.** Bull. New York Medical College 3: 83, 1940.

The application of hypertonic solutions of sodium chloride or barium chloride on the ventricular surface of dog hearts in situ causes extrasystolic allorhythmias and tachycardias which disappear within a few minutes. The same irregularities may be initiated with greater regularity by subepicardial injection of small quantities of the same salt solutions.

The structure of the barium tachycardias differs slightly from that of the sodium chloride tachycardias.

The rate of the tachycardias is increased by faradic stimulation of the left and especially the right stellate ganglion. Stimulation of the right or left vagus reinstitutes a tachycardia which has already disappeared or facilitates its appearance. The rate of a tachycardia appearing during and after vagus stimulation may be higher than that of the prevailing sinus rhythm.

Application of the same salt solutions to the sinus node tissue and auricular muscle bundles causes similar disturbances of rhythm. They are, however, remarkably rarer.

Even when fifteen active stimuli-forming centers were created at the same time by injections of barium chloride subepicardially, ventricular fibrillation never appeared.

Potassium chloride inhibits the formations of extrasystoles; they are rare after administration of solutions of calcium chloride.

The experiments prove the possibility of a rhythmic stimulus formation in the outer layers of the myocardium. They speak against the existence of a reentry mechanism as the cause of the extrasystoles and tachycardias, under the conditions described in this report.

AUTHORS.

**Ernstene, A. Carlton: Common Errors in Diagnosis of Heart Conditions.** Ohio State M. J. 36: 497, 1940.

Errors in cardiac diagnosis may be made either (1) by attributing symptoms to organic heart disease when no heart disease is present, or (2) by failing to recognize the cardiovascular origin of the patient's complaints. Mistakes of the first kind often result from incorrect interpretation of precordial pain or from failure to distinguish between true dyspnea and sighing respiration. Certain abdominal and intrathoracic conditions at times give rise to symptoms highly suggestive of coronary artery disease, and in a small group of patients with hyperthyroidism, cardiovascular symptoms and signs may so dominate the clinical picture that a diagnosis of some form of primary heart disease is made. The second kind of mistake most commonly results from failure to remember that gastrointestinal symptoms may overshadow all other complaints in certain cases of congestive myocardial failure or coronary artery disease. Less frequently, the

error results from overlooking significant physical findings in cases of valvular heart disease, chronic compression of the heart, or coarctation of the aorta, or from failure to appreciate the significance of the early symptoms of subacute bacterial endocarditis. The avoidance of these various errors depends upon thorough physical, roentgenologic, and electrocardiographic examination, and to an even greater extent upon careful analysis of the patient's symptoms.

AUTHOR.

**Goetz, Robert H.: Plethysmography of the Skin in the Investigation of Peripheral Vascular Diseases.** Brit. J. Surg. **27**: 506, 1940.

The author gives in detail the guiding principle and the detail of construction of different types of plethysmographs, together with the interpretation of the plethysmogram.

NAIDE.

**Berk, J. Edward: Circulation Time (Magnesium Sulphate Method) in the Diagnosis of Peripheral Vascular Disease.** Am. J .M. Sc. **199**: 505, 1940.

Through intravenous injection of 5 c.c. of 10 per cent magnesium sulfate solution, the arm-to-tongue and arm-to-extremity circulation times were determined upon 200 normal subjects and twenty-one patients in the general classification of peripheral vascular disease.

In general, individuals with peripheral vascular disease revealed a tendency toward a longer circulation time and a higher percentage of "blank" and "persistent blank" reactions. However, wide variations were obtained both in the normal and in the abnormal groups, and even in the same individual. Thus this method cannot be recommended for testing the efficiency of the peripheral circulation of a given patient.

SCHWARTZ.

**Jacobson, Edmund: Variation of Blood Pressure with Brief Voluntary Muscular Contractions.** J. Lab. and Clin. Med. **25**: 1029, 1940.

Experiments are conducted on eleven subjects with normal blood pressure and on four with chronically high blood pressure, all of whom relax at least fairly well upon request, whether through special training or otherwise. Electrical measurements are taken of contraction (action potentials) in various muscle groups, while blood pressure is recorded at certain times from the left upper arm.

In an individual otherwise relaxed, successive contraction of a muscle group or groups (for example, clenching one fist), for periods of several minutes or more, and then relaxing completely for similar periods, is frequently accompanied by corresponding rises and falls of systolic and diastolic pressures. The extent of the relative rise and fall depends not only upon the intensity of the particular voluntary contraction but also upon the degree and extent of relaxation present in the general musculature. No contrasting rise in pressure may be evidenced if the patient is not well relaxed before he clenches his fist. The addition of marked contraction in other regions (e.g., if he contracts muscles in the lower limbs or elsewhere at the same time as he clenches his fist) promotes further rise in blood pressure.

Under the conditions of the experiment, it is evident that emotional factors are reduced to a minimum or absent altogether. At the very least it seems safe to say that no more emotion is present when the subject clenches his fist or stiffens his legs than when he tries to relax. Evidently, therefore, emotional variations do not account for the variations in pressure which correspond with variations in

skeletal muscle contraction. The indications are that progressive tension in a muscle group tends to elevate systolic and diastolic pressures, and that this tendency increases if contraction spreads to other groups. Accordingly, the present findings lend further support to the view that in individuals with normal, as well as with increased pressure (essential hypertension), the pressure levels at any instant vary to an important and determinable extent with the magnitudes of contraction in the various skeletal muscles.

AUTHOR.

**Hiestand, W. A., Ramsey, Helen J., and Hale, Doris M.: The Effects of Cigarette Smoking on Metabolic Rate, Heart Rate, Oxygen Pulse, and Breathing Rate.** J. Lab. and Clin. Med. **25**: 1013, 1940.

Cigarette smoking caused an increase in metabolic rate in 82 per cent of thirty-nine subjects. In 13 per cent a decrease occurred. In 5 per cent no immediate effects were observed. The average effect on metabolic rate was an increase of 8.9 per cent. The maximum effect on basal metabolism of smoking one cigarette was reached immediately in some cases, and was delayed as long as forty-five minutes in others. The first rise in metabolic rate was typically followed by a second increase, reaching its summit about forty-five minutes later.

Smoking caused an increase in heart rate in 72 per cent of the persons, a decrease in 26 per cent, and no change in 2.5 per cent. After fifteen minutes the heart rate became slower than normal. The rate of breathing decreased immediately after smoking, returning to normal in about forty-five minutes. Smoking caused an immediate reduction in the oxygen pulse value, followed by an increase for at least forty-five minutes.

Greatest physiologic effects of smoking were shown by confirmed smokers who inhaled the smoke, and by persons who were unaccustomed to smoking. In this study, women showed more marked changes than men. More marked changes occurred in persons in a basal metabolic condition than in persons in a nonbasal metabolic condition.

AUTHORS.

**Leibel, Bernard: Peripheral Circulation by Photo-Electric Recording.** Brit. Heart J. **2**: 141, 1940.

An instrument for recording vascular changes in the tissues of the extremities and of the body surface has been described. Calibration has been made possible by the introduction of a photometer circuit; results are therefore both qualitative and quantitative. In addition an accurate estimation of the pulse velocity may be made by superimposing the electrocardiogram on the tissue circulation record.

The amplifier circuit described is relatively free from electrical distortion and mechanical and physical artifact have been controlled by adequate insulation. The instrument is self-contained and readily portable, and records may be taken without any previous preparation of the patient.

A series of typical records has been presented and briefly described. Some of these illustrate physiologic reactions to different stimuli, such as heat, excitement, asphyxia, and vasodilatation after amyl nitrite inhalation. The remainder of the records was obtained from cases of certain cardiovascular conditions. Examples of pulsus bigeminus, pulsus paradoxus, pulsus alternans, and the Corrigan pulse have been illustrated. Comparative estimation of the circulation in each of the limbs of a patient suffering from peripheral vascular disease has been included and the effect of the "Pavaex glass boot" has been demonstrated.

AUTHOR.

**Baer, Samuel, and Isard, Harold J.: The Value of the Ether Circulation Time in the Diagnosis of Right Heart Failure.** Am. J. M. Sc. 200: 209, 1940.

Ether arm-to-lung circulation times were done on 329 patients.

The ether time in 184 normal patients ranged from 3.5 to 9.4 seconds, with an average of 5.8 seconds. Only six of the 184 patients had times beyond 8 seconds.

In twenty-six patients with proven pulmonary disease, the ether time ranged from 2.5 to 10 seconds. The average was 6.1 seconds, and only two of the twenty-six patients had times beyond 8 seconds.

In ninety patients with cardiac disease, the ether time ranged from 4 to 19 seconds. The average in patients without heart failure was 5.8 seconds, in those with heart failure 10.2 seconds.

The ether test is of definite value in the diagnosis of right heart failure, and its differentiation from conditions simulating right heart failure.

AUTHORS.

**Kisch, Bruno, and Groedel, Franz M.: Changes in the Electrocardiogram Due to Local Cooling of the Chest Wall.** Cardiologia 4: 206, 1940.

After localized cooling of certain areas of the chest-wall of the human being, the electrocardiogram shows in suitable cases (large hearts, children) typical changes. First and most distinct are those changes observed in the chest leads. Cooling of the area of the heart apex, respectively the left ventricle, leads mainly to a change in the CR V lead (s-electrocardiogram), cooling of the chest-wall over the right ventricle to a change in the CR II lead (d-electrocardiogram). The reported observations show that in the human being thermic influence upon the heart surface can cause similar changes in the electrocardiogram, just as was found in animal experiments by Bruno Kisch, L. H. Nahum, and H. E. Hoff. At the same time the correctness of the explanation of the chest wall electrocardiogram given by Franz M. Groedel is proved again.

AUTHORS.

**King, E. S. J.: Regeneration in Cardiac Muscle.** Brit. Heart J. 2: 155, 1940.

Examination of a recent heart wound in a young adult was undertaken to determine the possible presence of myocardial hyperplasia.

This was demonstrated by: 1. The splitting of the fibers—as indicated by the size and arrangement of the fibers and their relationship to the capillary vessels. 2. Protoplasmic outgrowths from the ends of damaged fibers. 3. The presence of double nuclei in some fibers. 4. The presence of mitotic fibers.

This does not, however, presuppose that such hyperplasia is responsible for the healing of wounds, which occurs by the usual connective tissue proliferation and by the formation of scar tissue.

AUTHOR.

**van Bogaert, Adalbert, and Tombeur, A.: Scapular Atrophy and Angina Pectoris.** Cardiologia 4: 121, 1940.

The following syndrome can be observed in the course of hyperalgetic anginal crises. It is characterized by continuous pain in the axilla, restriction of active and passive movements of the scapular-humeral joint, atrophy of the deltoid and, occasionally, of the biceps muscle, and osteoporosis of the head of the humerus.

This syndrome is usually found in the left shoulder where the anginal pain irradiates.

The symptoms appear in the first weeks following the angina attack, sometimes later. The osteoporosis is not due to the immobilization of the scapular-humeral joint.

Vasomotor reactions were found on the affected side; there is usually vasoconstriction, sometimes vasodilatation, of the large arteries.

Similar symptoms were also found in cases of gastric ulcer with radiating pain into the left shoulder, furthermore in cases of cervical arthritis (C 4—C 6) and in cases of cervical ribs.

The scapular arthropathy is explained as the result of irritation of centrifugal sympathetic fibers in the roots of C 5—C 8.

AUTHORS.

**Gross, Louis: The Cardiac Lesions in Libman-Sacks Disease. With a consideration of its relationship to acute diffuse lupus erythematosis.** Am. J. Path. **16:** 375, 1940.

An extremely careful and detailed description of pathologic changes in the hearts of twenty-three fatal cases of disseminated lupus erythematosus is reported. Good photomicrographs are appended. The author demonstrates the presence of valvular and mural endocardial lesions typical of Libman-Sacks disease (atypical verrucous endocarditis) in at least eight cases. In all twenty-three cases lesions, which closely simulated four cases of Libman-Sacks disease, were present. Review of the literature since Libman and Sacks' paper shows clearly the clinical similarity between the disease described by them and the symptom complex which may be accompanied by cutaneous manifestations. Of Libman and Sacks' four original cases, two exhibited lupus. There is, Gross points out, a relatively acute febrile disease, often with signs of acute nephritis, often with purpura, with inflammation of the serous membranes, and with fatal outcome. At post-mortem examination, lesions of the heart similar to those described in this paper are found. These cases may or may not exhibit lupus erythematosus. His suggestion in nomenclature is that these two diseases be grouped as one and called Libman-Sacks disease. Note may be made of the presence or absence of cutaneous manifestations (disseminated lupus erythematosus). Several helpful points are listed for distinguishing this disease from certain cases of rheumatic fever and of subacute bacterial endocarditis.

STEELE.

**Gardner, John W., Mountain, George E., and Hines, Edgar A., Jr.: The Relationship of Migraine to Hypertension and to Hypertension Headaches.** Am. J. M. Sc. **200:** 50, 1940.

Migraine occurs approximately five times as often in a group of patients who have hypertension as in a group of nonhypertensive patients of corresponding age. The association of migraine with hypertension is probably influenced by genetic factors. Some patients experience a cessation of attacks of migraine prior to or coincident with the development of high blood pressure. This seems to be related more to the advancing age of the patient than to the onset of hypertension. Individuals who no longer have migraine headaches frequently experience those of the hypertension type. Those who retain their migraine are likely to have both types severely. An individual who has migraine is more likely to experience the hypertension type of headache than one not similarly afflicted.

AUTHORS.

**Dock, W.: Vasoconstriction in Renal Hypertension Abolished by Pithing.** Am. J. Physiol. **130:** 1, 1940.

On pithing the central nervous system of rabbits those with renal hypertension have a rapid fall of blood pressure to as low a level as normal controls. Even

holding venous pressure at high levels by intravenous infusion of acacia-Locke's solution fails to restore normal arterial pressure in these animals.

In pithed rabbits a rise in arterial pressure is easily evoked with epinephrine; the response is greater in those which have had renal hypertension for several months, but not in hypertensive rabbits nephrectomized thirty hours before pithing. No rise in venous pressure precedes the rise in arterial pressure. Renin, like epinephrine, causes a rise in arterial pressure in pithed rabbits, and thus differs from the humoral agent causing chronic renal hypertension. The latter apparently changes the reaction of the vasomotor center so as to maintain pressure at high levels. It also increases the sensitivity of the arterial response to epinephrine.

AUTHOR.

**Page, Irvine H.: Demonstration of the Liberation of Renin Into the Blood Stream From Kidneys of Animals Made Hypertensive by Cellophane Perinephritis.** Am. J. Physiol. **130:** 22, 1940.

Renin is liberated into the renal vein in increased amounts by the kidneys of dogs made hypertensive by cellophane or silk perinephritis, and by clamping the renal artery. Most of it disappears by the time the blood has reached the femoral artery.

Renin-activator is decreased in the blood from the renal vein and is increased in hypertensive animals when the femoral artery is reached.

Angiotonin-activator is not greatly decreased in the renal vein blood but may be increased in the femoral arterial blood in hypertensive animals.

Early in the course of malignant hypertension, large amounts of renin are liberated by the kidneys (one experiment). Later, both angiotonin-activator and renin-activator are greatly reduced or sufficient inhibitor is formed to abolish the reaction between them and angiotonin or renin (seven experiments).

AUTHOR.

**Page, Irvine H.: Difference in the Activating Effect on Normal and Hypertensive Plasma on Intestinal Segments Treated With Renin.** Am. J. Physiol. **130:** 29, 1940.

The reaction between renin and renin-activator is a specific one and the product of this reaction—angiotonin—causes strong contraction of isolated intestinal segments. This reaction has been employed to ascertain the renin-activating power of plasma.

Heparinized plasma derived from blood of some patients with essential hypertension causes greater renin-activation than does normal human blood. Plasma from dogs with experimental hypertension also exhibits this heightened power compared with plasma of normal dogs. This suggests that the humoral mechanism in the two types of hypertension have much in common and that the hypertensive either has increased amounts of renin-activator in the blood, or decreased amounts of renin-inhibitor, or both.

AUTHOR.

**Sweeney, H. Morrow: Do the Carotid Sinuses Exert a Pressor Activity When the Systemic Blood Pressure Is Low?** Am. J. Physiol. **130:** 186, 1940.

Lowering of the blood pressure in dogs anesthetized with chloralose to sustained low levels varying from 45 to 70 mm. Hg does not arouse any pressor activity in the carotid sinuses, which, if present, would be demonstrable by a fall in pressure when these areas were denervated. A gradual rise in pressure in ten of the

sixteen experiments indicates the presence of depressor activity at the time of denervation. In the other six there was no change in blood pressure.

AUTHOR.

**McCann, W. S.: Chronic Pyelonephritis: A Cause of Hypertension and Renal Insufficiency.** N. Y. S. M. J. **40**: 400, 1940.

Seven cases are described illustrating the importance and seriousness of mild or trivial urinary infections resulting in hypertension and ultimate renal insufficiency. The disastrous effects of pregnancy in such infections and their relation to the toxemias of pregnancy are illustrated by the first case.

The importance of doing pyelographic studies in patients with "essential" hypertension is stressed. Adequate treatment of mild urinary infection by chemotherapy, as well as a search for foci of infection, to prevent sequelae is urged.

SCHWARTZ.

**Reisinger, John N.: Dissecting Aneurysm of the Aorta.** Arch. Int. Med. **65**: 1097, 1940.

Four cases of dissecting aneurysm, with post-mortem examinations, are reported. In one case the diagnosis was made before death.

Two cases were observed for periods of three months and fourteen months, respectively. The changes present in the electrocardiograms and roentgenograms in these cases are discussed.

The absence of the typical pain of the syndrome was conspicuous in three cases, although in all cases severe symptoms developed rather abruptly.

There was severe progressive anemia in two cases.

The absence of intimal rupture in one case suggests that intramural changes may be important in the causation of dissecting aneurysms.

AUTHOR.

**Hertzman, Alrick B., and Dillon, John B.: Reactions of Large and Small Arteries in Man to Vasoconstrictor Stimuli.** Am. J. Physiol. **130**: 56, 1940.

The possibility of synergistic participation of the large arteries in the reactions of the small arteries and arterioles supplied by them, has been studied in man, on the radial artery-digital artery field, using the photoelectric plethysmographs, previously described, to record the reactions.

The responses observed involved spontaneous waves, the reactions to a deep breath, to the breath hold, to the cold pressor test, to loud noises and various psychic stimuli.

Radial artery participation in the vasoconstriction of the finger arteries was irregular and most obvious in instances of massive disturbances of the circulation. The degree of constriction of the finger arteries had little predictive value with respect to the occurrence of constriction in the radial artery. The data appear to show selection with respect to the participation, and with respect to the intensity of the participation, of the radial artery in the vasomotor responses of the small arteries and arterioles which it supplies.

AUTHORS.

**Dingle, Janet T., Kent, Gerald T., Williams, L. L., and Wiggers, C. J.: A Study of Alleged Quantitative Criteria of Vasomotor Action.** Am. J. Physiol. **130**: 63, 1940.

By use of simultaneous cardiometric records of the ventricles and mean arterial pressure in mildly ventilated, vagotomized dogs, data were obtained for calculating

peripheral resistance changes according to the formula $R = \frac{\text{mean pressure}}{\text{cardiac output per sec.}}$ in $\frac{\text{dynes. sec.}}{\text{cm.}^5}$, and comparing such values with the absolute and percentile changes in mean pressure.

Pressor effects on mean arterial pressure were induced in normal and "shock" dogs by reflex stimulation of the central vagus and phrenic nerves, by bilateral carotid compression, by use of epinephrine and pitressin.

The results, supported by previous tests on artificial circulation machines, strongly suggest that the quantitative estimation of changes in vasomotor tone of smaller vessels either by absolute or percentile changes in mean arterial pressures or by mathematical calculation of peripheral resistance is highly restricted even in experiments in which cardiac output is also measured. Mathematical calculations fail because mean arterial pressure, which enters into the formula, is affected by the relationship between systolic discharge and aortic capacity—but not, in our experience, by aortic elasticity. The formula does not take into account the aortic capacity in relation to systolic discharge either in the same animal or in animals of different sizes.

AUTHORS.

**Bunim, Joseph J.: Lupus Erythematosus Disseminatus.** Ann. Int. Med. **13**: 1399, 1940.

A case of lupus erythematosus disseminatus is reported in a white American girl, aged 20 years, who was observed over a period of twenty months from onset to termination of her illness. The patient exhibited most of the numerous features of the disease and was closely observed so that a fairly complete account of the natural history of the disease in this case was developed.

Clinically this case exhibited photosensitivity, cutaneous eruption, alopecia, arthritis, pericarditis, endocarditis, petechiae, papilledema, pleuritis, pneumonitis, nephritis, transient uremia, splenomegaly, hepatomegaly, ascites, peripheral edema, gastrointestinal disturbances, prolonged fever, anemia, leucocytosis, delirium, convulsions, and coma.

The significant findings at necropsy consisted of atypical verrucous endocarditis with superimposed bacterial endocarditis, adhesive pericarditis, disseminated vascular lesions, polyserositis, focal and diffuse glomerular nephritis, and interstitial pancreatitis.

MCGOVERN.

**Genzler, A. M., and Fox, T. T.: Disseminated Lupus Erythematosus a Cutaneous Manifestation of a Systemic Disease.** Arch. Int. Med. **65**: 26, 1940.

A well-studied case of lupus erythematosus occurring in a male, diagnosed ante mortem and confirmed by post mortem is reported. The pathologic material is presented together with photomicrographs of the characteristic lesions. The review of literature on this subject is well done.

MCGOVERN.

**Finkelstein, Reuben, and Jacobi, Mendel: Dissecting Aneurysm of the Aorta With a Case Report.** Ann. Int. Med. **13**: 1991, 1940.

A case of dissecting aneurysm of the aorta on the basis of arteriosclerotic changes, with some ideas compiled from the literature as to etiologic factors in this condition, is presented.

SCHWARTZ.

**Winternitz, M. C., and LeCompte, P. M.: Experimental Infectious Angiitis.** Am. J. Path. **16:** 1, 1940.

Various bacteria were introduced under aseptic technique into the adventitial tissue (more rarely on a thread into the lumen or into a doubly ligated stretch) of femoral, jugular, and carotid vessels of goats. By varying the virulence of the organism and the duration of the experiment, lesions of both artery and vein were obtained, ranging from acute suppurative and proliferative reactions with thrombosis to old, fibrous intimal plaques. A potential vascular pathway for passage of infection from vein to artery has been demonstrated in both goat and man by injection methods.

AUTHORS.

**Agress, Harry, and Smith, Margaret G.: Purpura Haemorrhagica Associated With Widespread Deposits of Crystalline Material: Reticuloendotheliosis.** Arch. Path. **29:** 553, 1940.

A case is reported of purpura hemorrhagica in which unique changes were observed due to the presence of crystalline material in the components of reticuloendothelial system and in other unrelated tissues. It is conjectured that this anatomic picture was the result of a metabolic disturbance and the possibility that the crystalline material was protein in nature was considered.

SCHWARTZ.

**Green, Harold D., and Gregg, Donald E.: The Relationship Between Differential Pressure and Blood Flow in a Coronary Artery.** Am. J. Physiol. **130:** 97, 1940.

The moment-to-moment rate of flow into coronary arteries was measured while the vessels were perfused under relatively constant heads of pressure.

Comparison of the rate of blood flow into a coronary artery with the differential pressure (difference between the perfusion pressure and peripheral coronary pressure) shows that: 1, the peripheral coronary pressures indicate the exact time relations of the changes of resistance to flow in the coronary arteries; 2, the systolic and diastolic values of these curves correctly represent the heads of pressure that will just not cause inflow of blood during the respective periods of the cardiac cycle; 3, the differential pressure curves represent the direction and roughly the magnitude of the phasic changes of coronary flow but underestimate the exact value of the moment-to-moment coronary flow.

The curves obtained indicate that under normal conditions (perfusion of the coronary artery with blood from the aorta) the intramural blood flow will show a sudden retardation with the onset of isometric contraction, during systole forward flow will persist in most hearts, with the onset of isometric relaxation forward flow will rapidly increase and will remain rapid during the latter part of diastole diminishing slightly with the decline of the head of pressure in the aorta.

AUTHORS.

**Gregg, Donald E., and Green, Harold D.: Effects of Viscosity, Ischemia, Cardiac Output and Aortic Pressure on Coronary Blood Flow Measured Under a Constant Perfusion Pressure.** Am. J. Physiol. **130:** 108, 1940.

The effects of several altered circulatory conditions on coronary flow have been studied during perfusion of the coronary artery with blood under a constant head of pressure. We have confirmed previous findings (using the method of differential pressures) that in elevation of blood pressure and increased cardiac output following augmented venous return, the coronary bed receives an increased

blood supply because, although the aortic pressure rises, the peripheral coronary pressure fails to rise as much. However, the increase of flow which actually occurs is generally somewhat greater than that predicted from the differential pressures.

In addition, the reduction in viscosity of the perfusate by substitution of Locke's solution for blood causes an unexpectedly large increase of flow—amounting at times to 300 to 400 per cent of the rate observed with blood. Also, a period of ischemia of the coronary bed greatly increases the flow during the initial period of restored circulation. Such flow augmentations are suggested by the concomitant slight decrease in peripheral coronary pressure, but the method of differential pressures fails to indicate the magnitude of the flow change.

It is concluded that peripheral coronary pressure curves can accurately represent the time relations of the change of flow to the aortic pressure variations but do not indicate the magnitude of the change in resistance to flow under various circulatory conditions; hence the flow itself is underestimated.

AUTHORS.

---

## Corrigendum

The title of the abstracted article by Benjamin A. Gouley on page 246 of the August issue of the Journal was incorrectly given. The corrected title and abstract are as follows:

**Gouley, Benjamin A.: The Myocardial Degeneration Associated With Uremia in Advanced Hypertensive Disease and Chronic Glomerular Nephritis.** Am. J. M. Sc. **200**: 39, 1940.

A peculiar type of myocardial degeneration appears to be intimately associated with the uremic and preuremic states of arteriolar nephrosclerosis and chronic glomerular nephritis. It is found especially in those patients who have cardiac failure. The latter may be the outstanding feature of uremic intoxication. Pericarditis may be regarded as a complication of this myocardiopathy.

AUTHOR.

# Book Reviews

RÖNTGENDIAGNOSTIK DES HERZENS UND DER GROSSEN GEFÄSSE: By Dr. Erich Zdansky, Vorstand der Röntgenabteilung am Krankenhaus Wieden in Wien. Wien, 1939, Julius Springer, 407 pages, 384 illustrations.

Roentgenologic examination of the heart and great vessels, and their relation to the lungs and mediastinum, is now a well-established procedure. It can be fully understood and appreciated only in conjunction with a sound knowledge of anatomy and pathology, and by correlation with clinical data in the broad sense of the word, i.e., by giving due consideration to constitutional factors, metabolic state, condition of the peripheral circulation, and to the functional status of the heart, as well as that of other organs.

Zdansky's book is an outstanding contribution. In addition to covering the subject very completely, it contains many fine original observations. The lucid presentation goes far beyond a description of roentgenograms; these are interwoven into a well-rounded, three-dimensional substance of clinical, physiologic, and pathologic observations. Thus the radiologist is revealed, not as a man solely absorbed with the technical interpretation of shadows, far removed from the bedside, but rather as a consulting physician.

It is a pleasure to state that a modern presentation of the subject of roentgenologic examination of the cardiovascular system is now available in three languages: Zdansky's book, in German; Laubry, Cottenot, Routier, and Heim de Balsac's *Radiologie Clinique du Coeur et des Gros Vaisseaux*, 1939, Masson et Cie., Paris, in French; and Roesler's *Clinical Roentgenology of the Cardiovascular System*, 1937, and *Atlas of Cardioroentgenology*, 1940, C. C. Thomas, Springfield, Ill., in English.

The quality of Zdansky's illustrations is of the high standard characteristic of Springer publications. Authors and editors in this country who may have been disappointed on seeing that the fine details of their original prints were lost in the process of reproduction—and this holds particularly true for roentgenograms and photomicrographs—ought to realize that the use of a screen with a fine grain is essential to faithful reproduction, in addition to good paper and careful, slow presswork. Insistence on this point will improve the quality of illustrations, although the cost is somewhat higher.

It is obviously impossible to do justice to Zdansky's book within the space available for a review. Only a few selected points will be considered.

Zdansky properly states that a carefully executed orthodiagram gives a more accurate estimate of absolute heart size than a teleroentgenogram, and he rightly warns against overrating the results obtained by kymography. The anatomic understanding of the roentgenograms presented in the three standard views is aided by beautifully colored schematic drawings. The importance of examining the heart in the right and left lateral recumbent positions, with a horizontal course of the roentgen rays, is stressed. A good explanation is offered for the plump appearance of the silhouette in infants and small children, with filling out of the waistline of the heart: the chest is deep and short, the angle of inclination of the heart—as seen in the lateral view—is relatively small, and the large vessels ascend less steeply than in older persons; therefore, in the anterior view, the silhouette appears to be foreshortened by projection, i.e., as if visualized somewhat from below. When speaking of measurement, the significance of the anteroposterior development of the heart is stressed, and it is pointed out that correlative measurements are of limited value because we are unable to express the development of the skeletal musculature

in mathematical terms, and the size of the heart is determined not only by its muscle mass, but also by the degree of filling, in which thickness and tonus of the heart muscle, heart rate, and venous return play a considerable role. Prolonged physical effort, including athletics, may lead to an increase in the size of the heart; this may be a physiologic process of adaptation, or a pathologic dilatation, and calls for clinical investigation.

With reference to heart disease, the author first discusses the radiologic features of enlargement of each of the four heart chambers, and stresses the functional aspects by referring to the inflow and outflow tracts of the two ventricles. The shapes of silhouettes and character of pulsations associated with the different types of valvular lesions are discussed. Reactivation of a rheumatic process in the heart is associated with hyperactive pulsations along the silhouette, and a rather acute increase in the size of heart may be observed; this, however, is reversible. Such an active endomyocarditis may well lead to heart failure, with no evidence of congestion of the lungs, as a rule. In cases of acute nephritis, with hypertension, the following interesting observations are made: Because of water retention, the diaphragm is abnormally high, and there is some pleural effusion on both sides; the cardiac shadow may be enlarged, often as a result of pericardial effusion; pulmonary edema of renal origin is present, and may escape clinical detection altogether, particularly when its location is chiefly central and interstitial. Zdansky has made interesting observations on the heart during the course of infectious and toxic conditions; he describes a latent dilatation which escapes detection when the size of the heart is studied with the patient standing up, but becomes apparent with the patient in the recumbent position: the dilatation is latent in the upright position because of inadequate filling of the heart as a result of peripheral vasomotor failure. There are good descriptions of the influence of anemia, metabolic disturbances, and vitamin B deficiency; also, ample space and illustrative material are devoted to cardiac aneurysm. For the radiologic diagnosis of chronic cor pulmonale, the value of the right anterior oblique view should perhaps have been stressed; in this view the prominence of the conus and the absence of left atrial enlargement are well demonstrated. Attention is directed to the inspiratory distention of the heart shadow which occurs in cases of emphysema and asthma, and also to changes in the silhouette caused by pleuropulmonary disease. Scoliosis with the convexity to the right causes a shift and rotation of the heart which give it a mitral configuration, whereas when the convexity is to the left there is an apparent widening of the aortic shadow. The funnel chest is responsible for a pseudoenlargement and mitral configuration of the cardiac silhouette. Intracardiac calcification is well illustrated.

Forty-four pages are devoted to a discussion of congenital malformations of the heart. The most interesting part is the explanation of that configuration designated as "coeur en sabot," which is associated with the tetralogy of Fallot. With this abnormality, the flow of blood in the right ventricle is diverted to the more right-sided aortic orifice, and hence an abnormal outflow tract is created, with its axis extending from the apical portion obliquely to the right, dorsad and craniad to the aortic orifice. Hence the waistline of the heart is not filled out, as would be the case with ordinary hypertrophy of the conus of the right ventricle, but is rather deepened, while the right ventricle projects to the left above the diaphragm and displaces the left ventricle dorsad. A case of tricuspid atresia shows what H. Taussig has described in this country. The different types of right-sided aortic arch are well covered, and the gourmand will enjoy the radiologic and anatomic description of the left-sided origin of the right subclavian artery.

In discussing pericardial effusion, Zdansky rightly points out the great difficulty of differentiating it from cardiac enlargement. With respect to the etiology of the effusion, some information may be obtained by observing the lung fields. An effusion of rheumatic or bacterial origin is not associated with pulmonary congestion. This may also hold true for the effusion of uremic origin, although the renal type of

pulmonary edema may be noted. In cases of effusion caused by cardiac failure, there will always be evidence of pulmonary congestion. In constrictive-adhesive pericardial disease, the cardiac shadow is either normal or moderately enlarged; marked enlargement is likely to be secondary to an associated valvular lesion, or to an encapsulated pericardial effusion. Irregularities in the contour may be characteristic, but mediastinal, interlobar, and diaphragmatic pleural thickening may give similar pictures. The amplitude of pulsations is much diminished, as a rule, although an increase, limited to the left side, is occasionally observed. He recommends testing for a change in the shape and position by studying the response of the mediastinal shadow to deep respiration, with the patient in the right and left lateral recumbent positions and with a horizontal course of the roentgen rays. Absence of a mediastinal shift in either position is indicative of mediastinal fixation, but this is also observed with other conditions, namely, bilateral pleural adhesions, a marked degree of cardiac enlargement, a large hydropericardium, pulmonary congestion, pleural effusions of considerable extent, and inability to take a deep breath. Calcification is the most conclusive evidence.

Special attention is devoted to the radiologic appearance of the lungs in cases of cardiovascular disease. An increase of pressure in the lesser circulation, such as may occur in connection with emphysema, kyphoscoliosis, pleural adhesions, or primary pulmonary sclerosis, is likely to exaggerate the arterial hilar shadows, and the pulsations of these vessels may be increased. The transparency of the lungs is not diminished. With pulmonary congestion the vascular structures become more marked, but their outline is less well defined, and the transparency of the lungs is diminished. Contributing to the characteristic appearance, there will be overfilling of the perivascular, peribronchial, and pleural lymphatics and hilar lymph-nodes, as well as transudation along the vascular and bronchial structures, or, in a circumscribed fashion, within the interstices and parenchyma. Small areas of atelectasis occur not infrequently. In the course of chronic pulmonary congestion caused chiefly by mitral lesions, multiple, small, dense nodules may be observed; they consist of true bone tissue. Chronic pulmonary congestion must be differentiated from chronic pulmonary edema. The latter occurs in connection with nephritis, essential hypertension, coronary artery sclerosis, aortic regurgitation, and mitral stenosis. It is not diagnosed clinically, as a rule, because of its central location and because it is exclusively or predominantly interstitial. It does not reveal a vascular pattern, such as is seen with the ordinary variety of pulmonary congestion, but is characterized by cloudy, inhomogeneous opacities, which, as a rule, leave free the apical and axillary portions of the lungs. Periarteritis nodosa may produce a similar picture.

Measurement of the aorta is made chiefly by the Kreuzfuchs method, i.e., in the anterior view the distance between the outermost point of the aortic knob and the left lateral contour of the barium-filled esophagus is ascertained. The width of the arch is thus measured. When there is elongation of the aorta, or a spread of the aortic loop caused by a high position of the diaphragm, the patient may have to be rotated slightly towards the right anterior oblique position. The average measurement for the healthy adult between the ages of 20 and 50 is 2.5 cm., with values as low as 1.8 cm., and as high as 2.8 cm. for the oversized person. Starting with the sixth decade, measurements of 2.7 to 3.0 cm. are still within normal limits. The amplitude of pulsations along the aortic shadow does not permit one to draw conclusions regarding the anatomic condition of the wall, for vascular tonus has much to do with these pulsations. Large pulsations occur when the vascular tonus is low, as in aortic regurgitation, active endocarditis and other infectious diseases, severe thyrotoxicosis, tabes dorsalis, Addison's diseases, and disturbances of blood pressure regulation; but in nephritic patients who have a high vascular tonus, the pulsations may be very small. Diffuse dilatation of the aorta may be caused by syphilis, as well as by atheromatosis. The former should be thought of when the patient is

middle aged and the heart is not enlarged. Calcification occurs with both syphilitic aortitis and atheromatosis. Diffuse elongation of the aorta, without appreciable dilatation, is caused by atheromatosis, without any elevation of blood pressure. An isolated dilatation of the ascending aorta is suggestive of syphilitic aortitis, but is not characteristic because it is also noted with arterial hypertension and aortic regurgitation and stenosis. Finally, the diagnosis and differential diagnosis of aortic aneurysm are discussed in detail.

Zdansky's book is an outstanding contribution and should be studied by anyone interested in the cardiovascular system who has a reading knowledge of German.

HUGO ROESLER

BAINTON AND BURSTEIN'S ILLUSTRATIVE ELECTROCARDIOGRAPHY: By Julius Burstein, M.D., Associate Electrocardiographer and Chief of the Cardiac Clinic, Morrisania City Hospital, New York, N. Y. Second edition, 1940, 277 pages, 106 plates, D. Appleton-Century Co., New York and London, $5.00.

The first edition of this book was regarded by one reviewer (AM. HEART J. **10**: 566, 1935) as the best answer to the question, "What shall I read to learn something about electrocardiography?" In the opinion of the present reviewer, the second edition deserves a similarly hearty recommendation, in spite of the fact that the author ignores parasystole, the relatively common form of right bundle branch block described by Wilson, et al. (AM. HEART J. **9**: 459, 1934), and the electrocardiographic changes which may be caused by pericardial effusion. His incorporation of numerous normal and abnormal precordial leads, together with the reports of the British and American committees which were appointed to recommend standard procedures for obtaining such leads, enhances the value of the book greatly.

Unfortunately, the English, especially the punctuation, leaves much to be desired. Perhaps such a barbarous neologism as "diphasism" will some day become respectable, but, at the moment, it produces in the reader the same uncomfortable feeling as does the expression "isoelectricity of the T wave."

The unconventional format lends itself well to the author's method of presenting his material, but it is the bane of librarians, and it makes the book hard to hold in one's lap.

HORACE M. KORNS

# American Heart Association, Inc.

RADIO CITY

50 WEST 50TH STREET, NEW YORK, N. Y.

DR. WILLIAM D. STROUD
*President*

DR. PAUL D. WHITE
*Vice-President*

DR. HOWARD B. SPRAGUE
*Secretary*

DR. WALTER W. HAMBURGER
*Treasurer*

## BOARD OF DIRECTORS

| | | | |
|---|---|---|---|
| DR. T. HOMER COFFEN | Portland, Ore. | *DR. EDWIN P. MAYNARD, JR. | Brooklyn |
| DR. CLARENCE DE LA CHAPELLE | New York City | DR. THOMAS M. MCMILLAN | Philadelphia |
| DR. WILLIAM DOCK | San Francisco | DR. JONATHAN MEAKINS | Montreal |
| DR. HUGH FARRIS | St. John, N. B., Canada | *DR. FRANKLIN NUZUM | Santa Barbara |
| DR. WALTER W. HAMBURGER | Chicago | DR. STEWART R. ROBERTS | Atlanta |
| DR. GEORGE R. HERRMANN | Galveston | *DR. ROY W. SCOTT | Cleveland |
| *DR. EMMET F. HORINE | Louisville | *DR. HOWARD B. SPRAGUE | Boston |
| DR. T. DUCKETT JONES | Boston | *DR. WILLIAM D. STROUD | Philadelphia |
| *DR. EMANUEL LIBMAN | New York City | DR. LOUIS VIKO | Salt Lake City |
| DR. DREW LUTEN | St. Louis | *DR. PAUL D. WHITE | Boston |
| DR. GILBERT MARQUARDT | Chicago | DR. FRANK N. WILSON | Ann Arbor |
| *DR. H. M. MARVIN | New Haven | *DR. IRVING S. WRIGHT | New York City |
| | | DR. WALLACE M. YATER | Washington, D. C. |

DR. H. M. MARVIN, *Chairman, Executive Committee and Acting Executive Secretary*

GERTRUDE P. WOOD, *Office Secretary*

TELEPHONE CIRCLE 5-8000

THE American Heart Association stands alone as the national organization devoted to educational work relating to diseases of the heart. Its Board of Directors is composed of twenty-five physicians representing every portion of the country.

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning circulation of blood and lymph. Any physician or investigator in good standing may become a member of the section after election to the American Heart Association and payment of dues to that organization.

To coordinate and distribute pertinent information, a central office is maintained, and from it issues an ever widening stream of books, pamphlets, charts, posters, films, and slides. These activities all concern the recognition, prevention or treatment of the leading cause of death in the United States, diseases of the heart. The AMERICAN HEART JOURNAL is under the editorial supervision of the Association.

The income from membership and donations provides the sole support of the Association. Lack of adequate funds seriously hampers more widespread educational and research work imperative at this time. Great progress has been made, but much remains to be done.

Annual membership is $5.00 a year and journal membership at $10.00 includes a year's subscription (January-December) to the AMERICAN HEART JOURNAL and annual membership in this Association. A cordial invitation to join in this crusade is extended to you.

The American Heart Association solicits your support to the end that it may continue more effectively the campaign to which it has devoted all its energy.

---

**Executive Committee.*